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# Boletín

*de la*

## Asociación Médica de Puerto Rico

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VOL. 56

ENERO, 1964

NO. 1

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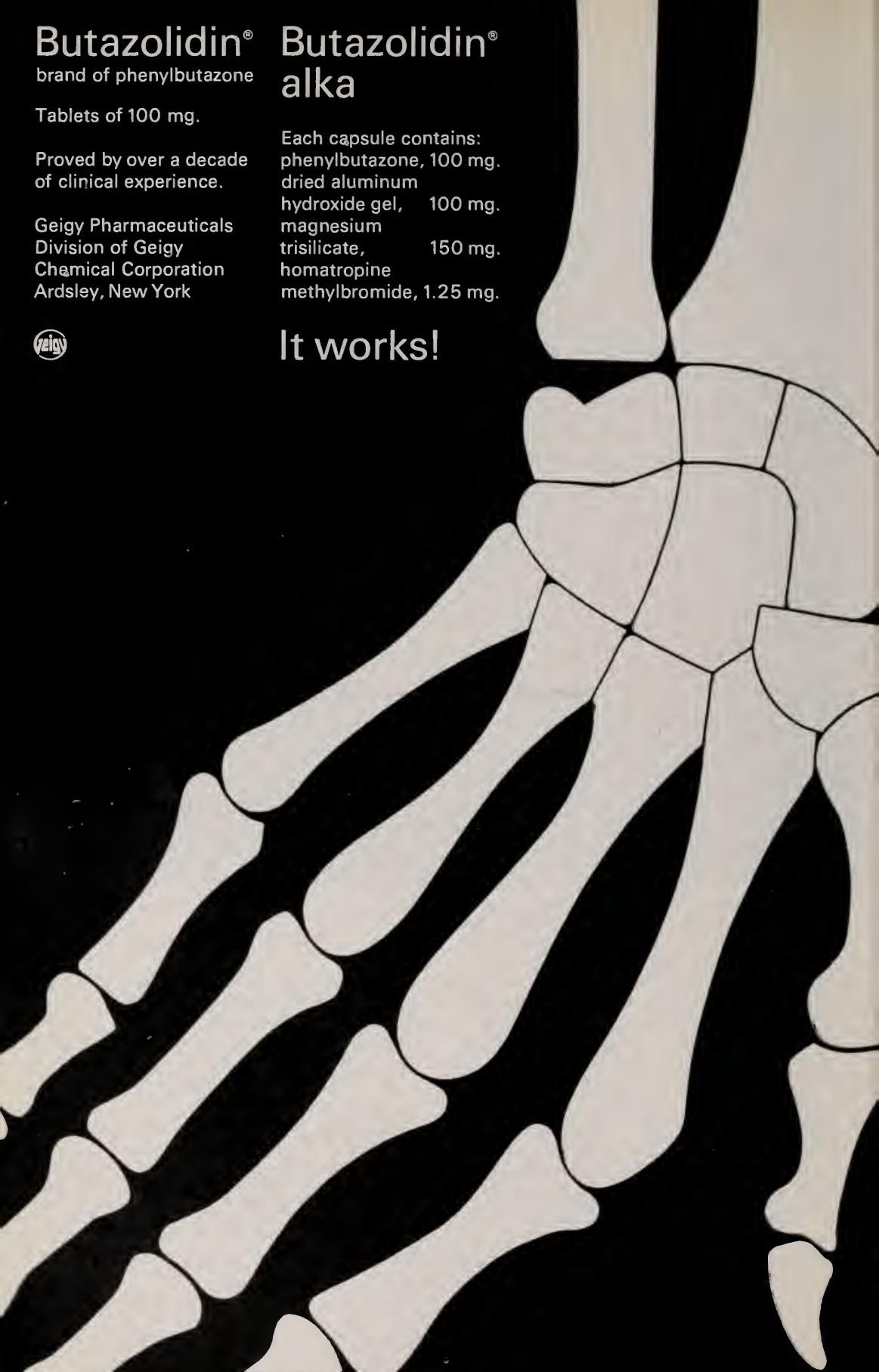
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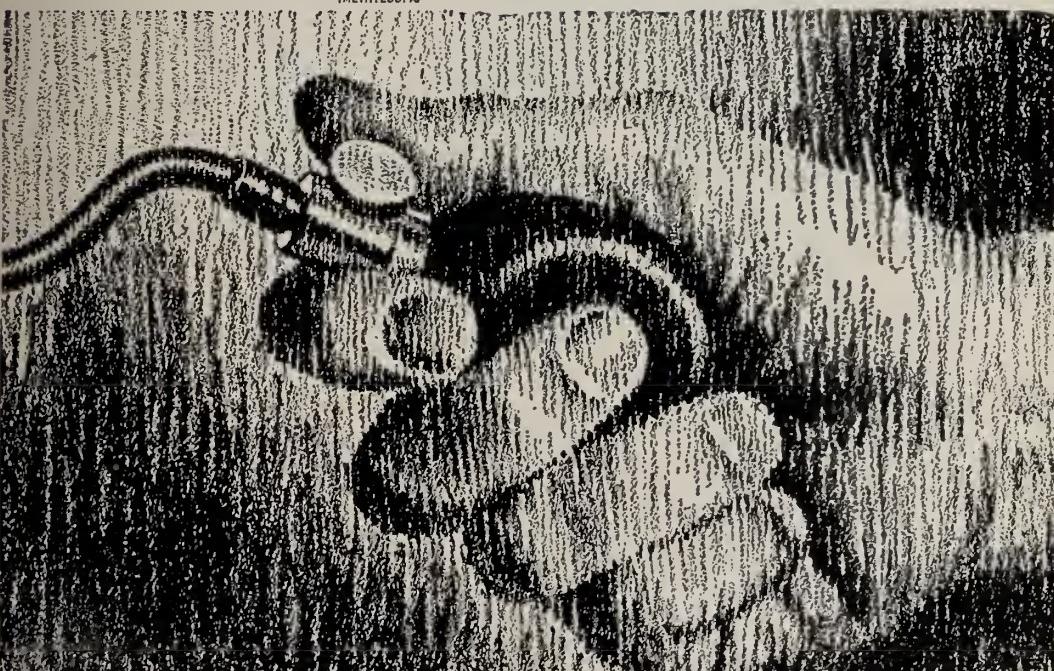
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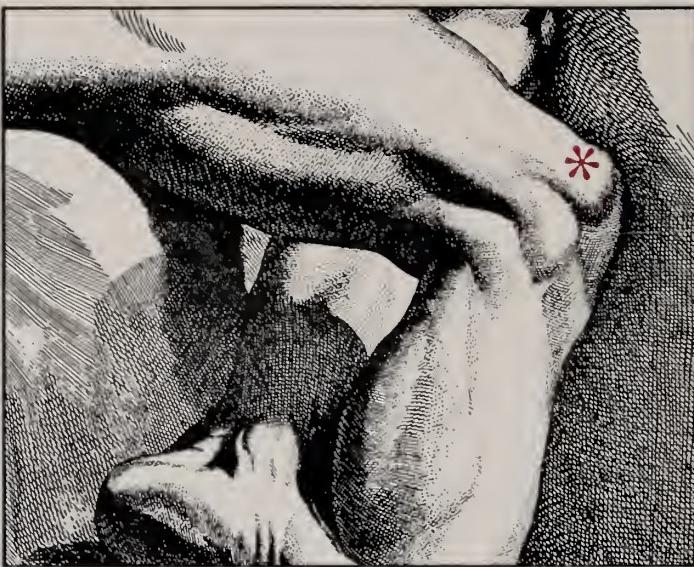
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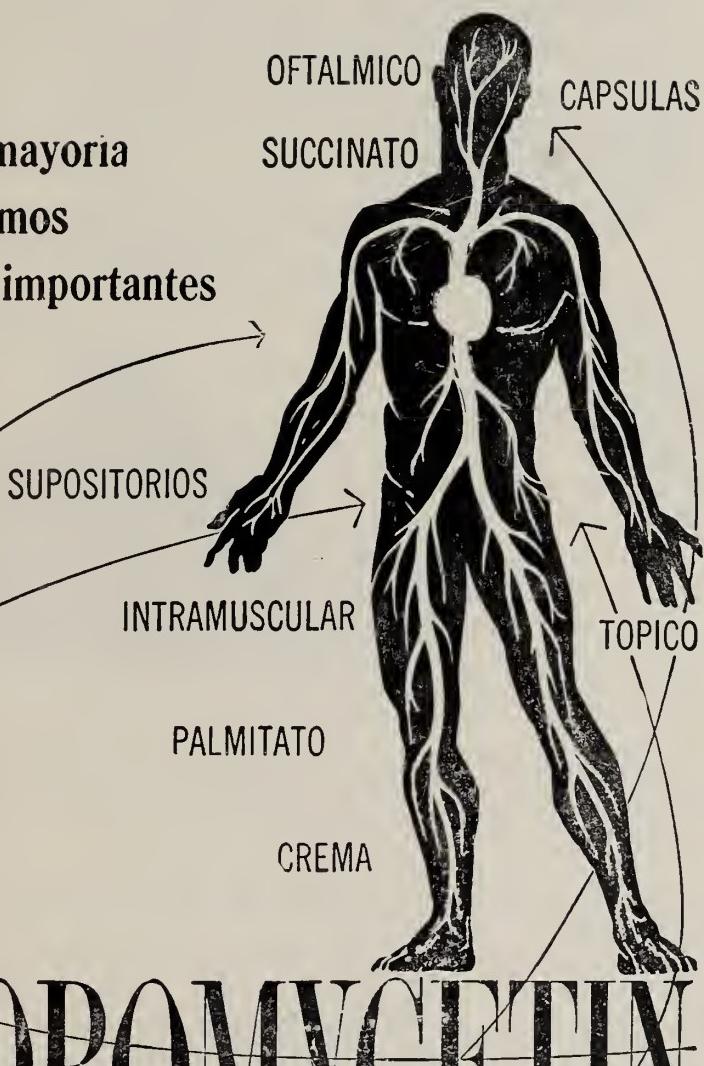
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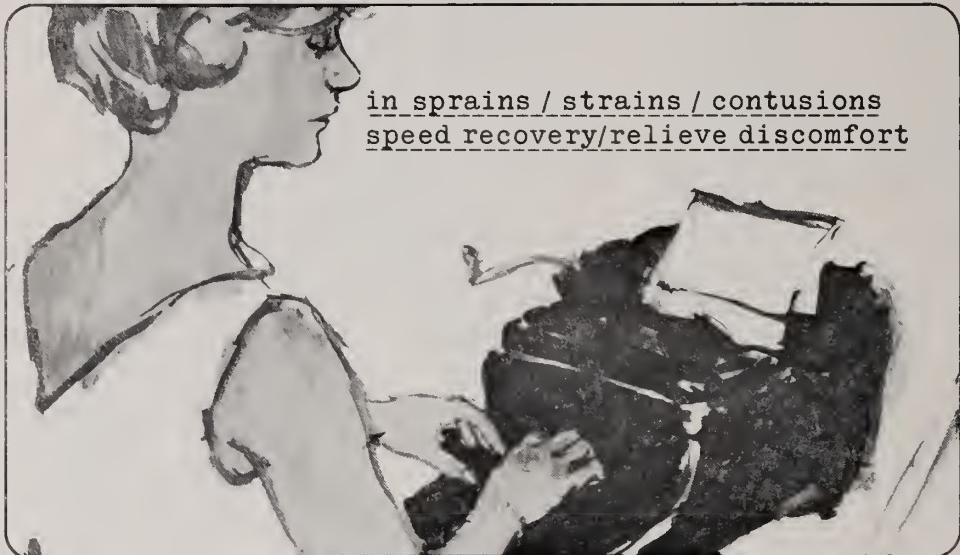


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# BOLETIN

DE LA ASOCIACION MEDICA DE PUERTO RICO

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## OUT PATIENT TREATMENT OF ACUTE SCHIZOPHRENICS

J. A. NUÑEZ LOPEZ, M.D.\*

### Introduction:

During recent years there has been an increasing tendency to treat schizophrenics as out patients. This has been due largely to the fact, among other reasons, that more patients are now seen in the early stages of the disease and as follow ups after hospitalization.<sup>1</sup>

Although many psychotic patients are still hospitalized for environmental reasons, (parental attitudes, inability to come for treatment, no family at all), most of the patients are hospitalized to protect them from their uncontrolled or inappropriately controlled aggressive impulse toward themselves, as in suicidal tendencies, or toward others. But with the use of ataractic drugs the aggressive tendencies of these patients are usually so rapidly controlled that we can avoid hospitalization in an increasing number of psychotics.<sup>2</sup>

In this way we can avoid the complications inevitably inherent in the hospitalization of a psychiatric patient. The disadvantages of hospitalization have been summarized by Fourby<sup>3</sup> as follows: "Withdrawal from others is recognized as most devastating for the personality, but it has also been learned that withdrawal can be fought successfully along psychotherapeutic lines, and that it is easier to prevent it than to fight it."

"The more nearly normal the environment, the better for the patient. The community with its many possibilities of interpersonal contact is therefore generally better for the patient than the artificial hospital environment. One conclusion from this is that schizophrenic patients generally should be discharged as soon as the acute symptoms which had made admission necessary had

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\* From the Department of Psychiatry, School of Medicine, University of Puerto Rico, San Juan, P. R.

been suitably treated and are under control. In this manner the writer thinks, deterioration can be adverted in most cases."

How hypersensitive acute schizophrenics may be unconsciously led into antitherapeutic direction in some psychiatric hospitals is discussed by Lehman.<sup>4</sup> He also mentions statistical evidence to suggest that the longer the psychotic patient remains in the hospital, the poorer are his chances for ever returning to useful functioning. Davis,<sup>5</sup> who considers motivation as the most important single factor in therapeutic success with schizophrenics, finds it affected adversely by hospitalization.

Considering the possibility that in very ill hypersensitive young schizophrenics, no admission at all could be better than short hospitalization, we decided to treat them as out patients in the Río Piedras Out Patient Clinic of the Mental Health Program of Puerto Rico.

#### Material:

Cases were limited to young adult schizophrenics (age span 18-26 years) having their first attack, who had not previously received professional treatment and who showed no gross evidence of organicity. Further selection criteria were that they live in the metropolitan area, so that transportation to the Clinic would be easy and that at least one parent be available to care for the patient while at home.

Care was taken to select cases whose diagnosis was obvious and who were so disturbed that they would ordinarily have been hospitalized.

The personnel consisted of the writer as therapist, a social worker and the referring physicians (staff psychiatrists, second and third years residents). Although the therapist was assigned to the clinic on a half-time basis, arrangements were made so that he was always available to these patients. Home visits were made by the therapist when necessary. The social worker visited all the patient's homes and interviewed all available parents.

Physical examination was performed on all patients, the males were examined by the therapist and the females by the general practitioner of the Clinic. Laboratory studies were limited to C.B.C., urinalysis and serological tests for syphilis which were done during the first visit. Psychologic evaluation was done on two of the patients.

The parents were seen by the social worker and the therapist who had frequent short interviews with them. In these interviews (almost always immediately after having seen the patient) the therapist investigated the patient's progress at home, their

reaction to current events; oriented their parents in relation to the administration of drugs and the desired general attitudes toward the patient as well as how to manage special situations that would arise at home.

We encouraged them to try to solve their problems themselves by conveying the feeling that they were part of a team that was working to help their son or daughters get well. This was done regardless of how "sick" the parents seemed to be.

During a four month period eight cases fulfilling the above mentioned screening criteria were referred.

#### CASE SUMMARIES

##### Case 1:

A twenty two years old, white, male electrician who three months prior to admission started to feel weak, with a "bothering sensation in my stomach" had quit work, developed ideas of reference, spent hours looking at himself in the mirror or just "lying in bed", isolated himself, developed fear of any interpersonal relations and had visual and auditory hallucinations.

When he was admitted he looked tense, his eyes were wide open, his affect was flat but he was logical, coherent, and relevant. He was partially aware of the unreality of the hallucinations, delusions and ideas of reference which he had exhibited openly four days before with the referring physician.

He was started on trifluoperazine (Stelazine) 2 mgs. b.i.d. and was seen two or three times a week. After one month of combined psychotherapeutic and ataractic treatment he started working part time as an electrician and the symptomatology was completely under control. Throughout his therapy he resisted talking about his disease. For about four months he came regularly for therapy but for the last five months he came only sporadically to the clinic. He remained free of symptoms and no longer needed ataractics.

##### Case 2:

An eighteen year old, white male, a high school student, who three months prior to admission had quit school when he started "to walk around the neighborhood without getting any place". He felt he was losing his mind and developed suicidal and homicidal ideas along with visual and auditory hallucinations, insomnia and crying spells.

On admission he was frightened, with no variation in affect

and showed evidence of ideas of reference, suicide and homicide. He reported visual and auditory hallucinations.

He was seen two to three times per week for three weeks and was treated with trifluoperazine (Stelazine) 2 mgs. b.i.d. After six weeks of treatment he started working with his father as a carpenter. His symptoms gradually disappeared and except for occasional headaches he has been well for the last four months. He still working and is now planning to study drafting. He has received no ataractics for the last two months, but has continued coming for psychotherapy.

#### Case 3:

A twenty year old white female law student. One month prior to admission after going to a dance where a classmate held her hands in the presence of her fiancée, became excessively preoccupied about the incident. At her home she developed ideas of reference and persecution. She acted as though she could guess other people's thoughts and became markedly frightened about going out of her home.

On admission she showed perplexity and occasional crying. There was evidence of prelogical thought and clang associations. She was verbose, circumstantial and irrelevant. There were mystical delusions and she reported auditory and visual hallucinations.

She was seen every two days and was started on Stelazine 2 mgs. b.i.d. This was changed to thioridazine (Mellaril) 50 mgs. t.i.d. as she developed pseudoparkinsonism. She gradually improved and in six weeks she was in such a good condition that we let her return to two classes which she handled without difficulty.

Since then she has continued studying and doing good work. She is seen once weekly but still shows resistance to talk about her feelings. She has been without ataractics for four months now and is in complete remission of symptoms.

#### Case 4:

This eighteen year old, white female, student developed symptoms two weeks prior to admission. After attending a dance with a friend, she started crying, developed visual hallucinations and ideas of persecution. She thought the world was close to its end, became irrelevant and incoherent, went out of her home and had to be located by the police. During interview she showed perplexity, negativism, psychomotor retardation with blunt affect. There was blocking and she admitted delusions and other "rare

things". She was seen twice a week for the first month and treated with trifluoperazine (Stelazine) 3 mgs. b.i.d. which was later changed to Mellaril 50 mgs. t.i.d.

For the past three months she has shown almost no pathologic symptoms. She has assumed complete responsibility for the house work but refuses to resume studying and has demonstrated continued resistance to treatment.

Psychological evaluation of this case supports the therapist's impression that this girl showed manic-depressive rather than schizophrenic pathology.

#### Case 5:

This twenty six year old female secretary eleven months prior to admission after rejecting a job that some friends had gotten for her began to feel guilty, developed persecutory and omnipotence ideas. She believed people could read her thoughts and received orders by telepathy. She refused to get out of her room and believed somebody was going to do "some harm" to her.

When first seen nine days after having been started on thioridazine 25 mgs. t.i.d. by the referring physician she entered the office crying and with some flatness of affect between crying spells. However, at this time she spoke of the above mentioned secondary psychotic symptoms as things of the past. Two months later, after five interviews she was working and symptom-free. She is now coming every two weeks and is still taking thioridazine (Mellaril) 25 mg. t.i.d.

#### Case 6:

A twenty five year old, negro, single male who for the six months prior to his first clinic visit had shown periods of psychomotor agitation alternating with ones of aloofness and perplexity in which he just stared and occasionally cried had developed a marked tendency to isolation, ideas of reference and irrelevant speech.

On the first interview he showed affective flatness, psychomotor retardation, autism, and answered only in monosyllables. On occasion he just stared with his eyes wide open and with marked perplexity, as if he were hallucinating.

While the therapist was interviewing his mother, the patient wandered out of the clinic but managed to reach his home several hours later. He was treated with ataractics intramuscularly and was seen only once more at the clinic as his mother claimed she had no money to bring him. Before a home visit could be made

he developed an acute exacerbation of a chronic glomerulonephritis for which he had to be hospitalized.

He was treated with five elective shock treatments ataractics and discharged after two months of hospitalization. Four months after discharge he still shewed marked flatness of affect, psychomotor retardation, with no initiative, spending most of the time "thinking" at home without interest in his surroundings. He got worse and was re-hospitalized.

#### Case 7:

This twenty one year old, white male who for the last two years had been limiting his activities and remaining daily after work at his church till midnight developed severe anxiety after getting married, one month prior to admission. His sexual relations were unsatisfactory as he suffered premature ejaculations. Three weeks later, his boss had called his attention to an absence, he developed an attack in which he cried, screamed and repeatedly tried to run away from home. Later he developed attacks of psychomotor agitation alternating with periods of perplexity, hallucinations and insomnia. He abandoned his personal care, refused to eat and occasionally was destructive.

On admission he appeared with a long beard, showed psychomotor retardation, flattened affect, perplexity, and on occasions made grunting sounds as he jumped in his chair. He was in panic, hallucinating, and showed irrelevance and mystical delusions. When he experienced block he described it as a feeling of "I fall in an empty space."

He was referred to the author after the family had given the consent for hospitalization, for the referring physician was not aware of our program. In the first interview the family was resistant to having the patient at home and six days later the patient was hospitalized by another therapist after he had tried unsuccessfully to reach me by phone.

The patient was treated at the hospital with ten electric shock treatments had a partial remission of symptoms and has since been readmitted on two occasions.

#### Case 8:

This twenty year old, white male for the last three years prior to admission to O.P.D. had been suffering from "bad thoughts" such as killing himself, hallucinations and ideas of persecution and references. These symptoms got worse to the point of his remaining in his room reading the Bible "to purify himself."

From the beginning we had problems with attendance to the clinic as he lived alone with his grandmother and he never accepted the idea of being ill. His father, who had re-married, brought him in occasionally; his mother was living in New York and never asked about him.

We visited him several times trying to motivate him without success. When his father stopped bringing him to the clinic he got worse and his sister then decided to take him back to New York even though we offered him hospitalization. At that time he showed a clear picture of paranoid schizophrenia.

#### Treatment:

The treatment consisted basically of psychoanalytically oriented psychotherapy and ataractis. During the acute stage of the disease the patients were seen twice a week but they, as well as their parents, were informed that we were available 24 hours a day. Also it was made clear that if for any reason the parents were unable to bring the patient to the hospital we would visit them at home whenever needed. Although these extra services were offered, none of the patients made use of them except for an occasional extra visit to the clinic during regular working hours.

Home visits were made by the therapist to motivate two of the patients. The social worker visited all of them.

Trifluoperazine (Stelazine) (not over 6 mgs. daily) and thioridazine (Mellaril) (not over 300 mgs. daily) were the ataractics used. All patients were started on one of these drugs by the referring physician and almost all had shown some improvement of the acute symptomatology when we saw them for the first time after three to four days of chemotherapy.

The following points were considered in our approach and management of these patients in the acute stage of the disease:

1) From the first contact we considered the patient oversensitive with very intense inner affective experiences<sup>2,7,8</sup> no matter how disturbed they appeared to be.

2) Also from the first contact they were considered capable of communicating by themselves and of controlling their overwhelming emotions. The patients were seen alone and before talking to the family. On occasion during the first interview they become so excited that they needed help other than the presence of the therapist to control themselves. In this case after asking the patient's preference one of the parents was included temporarily in the interview.

3) Very early they were stimulated to express what was hap-

peming, what they were feeling and to relate this "feelings" to events, thoughts and to early or distant fantasies.

4) No details were asked about secondary symptoms such as delusions and hallucinations. In fact, they were discouraged from using them as they interfered with their communication. The patients were confronted with the secondary symptoms only if these consistently reappeared every time they talked about a specific topic.

#### Comments:

Comparative studies with a larger number of patients over long periods of time are needed in order to prove the advantages of treating acute schizophrenics at an out patient level. From our limited study we have obtained the following impressions:

1) If cooperation from the patient's family is obtained and if we offer 24 hours service a day as our medical colleagues do with other patients in failure (cardiac, diabetic, etc.) acute psychotics can be successfully treated at the out patient level.

2) As responsibility for treatment is not taken completely from the patient, his already low self-esteem is less affected, no excessive dependency is fomented and a feeling of mastery over his own impulses is more rapidly felt as the patient is stimulated to use earlier his own healthy resources. Consequently, convalescence is shorter and rehabilitation made easier.

3) Since the families are used more intensely as part of the therapeutic team, they have a better opportunity to "do something for sons or daughters", they feel less guilty and later have less tendency to overprotect them. Overprotection that sometimes interferes with the rehabilitation of the patient.

4) As the families are exposed to the patient's exaggerated reactions to their attitudes they can be easily confronted with these attitudes and there is a better oportunity to improve them. At the same time they are confronted with the attitudes of healthier members of the families, attitudes which sometimes can be "taught" to them.

5) As the patient is more aware of the course of recovery<sup>2</sup> and is still in contact with some of the precipitating agents, he can see in a more intense way how the symptoms are precipitated by anxiety (psychic pain) and "learns" faster to avoid them, whether by the use of ataractics or by means of his relation with the therapist or both. It is also felt that motivation for further psychotherapy is less affected.<sup>10</sup>

6) Even in cases in which the admission can not be avoided, as when the family does not cooperate or there is no family at all,

we feel that the ideal place for treatment will not be the large psychiatric state hospital (no matter the temporary advantages) but in a general hospital ward where the patient will be treated as a person who is temporarily in physiologic decompensation of the central nervous system. There he can mingle with other physically sick persons, but whose reality testing is better than those of the mental patient.

#### SUMMARY

In five of eight young patients experiencing their first psychotic episode the acute symptoms disappeared during the first month of out patient treatment. After one and a half month of treatment, three of them were working, one began studying law and one was working at home. Five months later this improvement was maintained. At this time four of them were no longer taking ataractics but had shown resistance to long term psychotherapy.

The three who did not respond favorably really represent in part a poor screening in that they had actually been showing symptoms for years prior to admission to our clinic. Two of them had to be hospitalized, one for medical reasons, the other largely because of inappropriate management of the first contact. This we find to be of utmost importance.<sup>2</sup> The third patient was removed from our program by a very uncooperative family.

Considering the above-mentioned evidence and although the number of patients is too limited to justify any far reaching conclusions, it is our impression that acutely ill young schizophrenics with a first attack of short duration (not over one year) can be successfully treated in the psychiatric out patient department.

#### SUMARIO

Ocho pacientes que sufrían su primer brote psicótico se trataron en la Clínica Externa del Hospital de Psiquiatría de Río Piedras. Cinco de estos pacientes respondieron favorablemente al tratamiento que consistió de psicoterapia y farmacoterapia. Tres pacientes no respondieron al tratamiento. Todos ellos habían sufrido síntomas por años.

Considerando los resultados arriba expuestos y aunque el número de pacientes es limitado para llegar a conclusiones definitivas es nuestra impresión que pacientes esquizofrénicos agudos con su primer ataque de corta duración (no más de 1 año) pueden tratarse en Clínica Externa si se les ofrece servicios de 24 horas.

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## REPAIR OF DEFECTS IN THE TENDO ACHILLIS\*

E. BLAS FERRAOULI, M.D.

C. JOSE FERRAOULI, M.D.

The purpose of this paper is to emphasize the marked disability produced by neglected or poorly treated ruptures of the Achilles tendon; and to present our experience with a modification of the original Bosworth's procedure as presented at the Orthopedic Section of the New York Academy of Medicine, February, 1955<sup>2</sup>.

Although our experience is limited to seven cases since 1956, the results obtained are so satisfactory that we strongly recommend this procedure, not only in the treatment of delayed ruptures of the tendon, but also in fresh ruptures where a defect is present and an end to end primary repair is not possible. Only six cases are included in this preliminary report.

Rupture of the tendo achilles usually occurs in early life in three ways: laceration by cutting by a sharp instrument; blunt external trauma; sudden contraction of the calf muscles.

Achillis tendon rupture produced by a sudden contraction or muscle violence occurs when the foot is in extreme dorsiflexion and the tendon is taut. This can occur while playing basketball, tennis, handball, and in sprinting. About 300 cases have been re-

\* From the Surgical Services State Insurance Fund and the Veterans Hospital, San Juan, P. R. Presented at the P. R. Chapter American College of Surgeons, 1963.

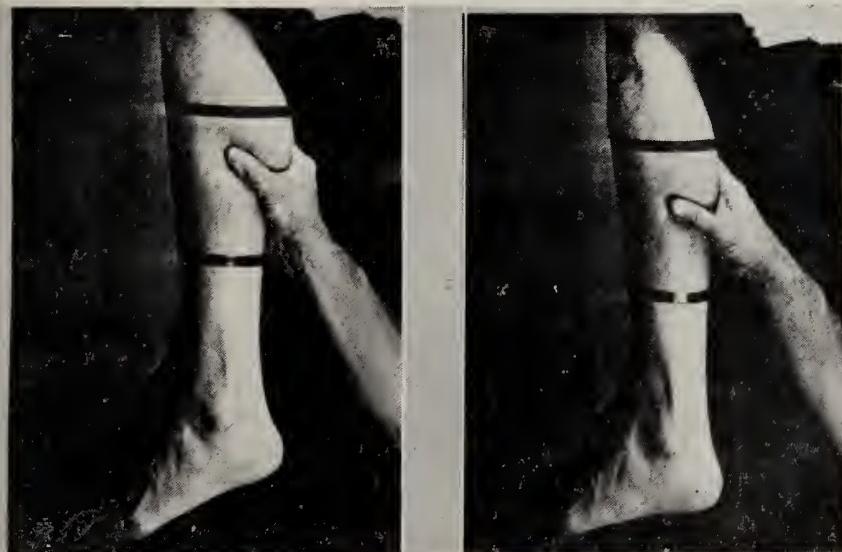


Figure 1

Squeeze test of Thompson (3). Normal reaction.

ported since Ambroise Paré first described this condition in 1575. The rupture of the tendon usually occurs about one and a half inches above its insertion in the os caleis. The physical signs are: a gap which is palpated and increased by dorsiflexion of the foot; retraction of the proximal end of the tendon and swelling of the muscles; loss of push-off; loss of active plantar flexion; and non-reaction to squeeze test (Thompson) (Fig. 1) which is performed in the following manner: the patient lies in the prone position on a table with his feet reaching over the end or he kneels on a chair. The calf muscles are squeezed in the middle third. Absence of plantar movement or flexion of the foot indicates rupture of the heel cord. It has also been shown experimentally and at operation that rupture of the Soleus muscle alone interferes only with the continuity of the heel cord and is only responsible for the passive flexion of the foot.<sup>8</sup>

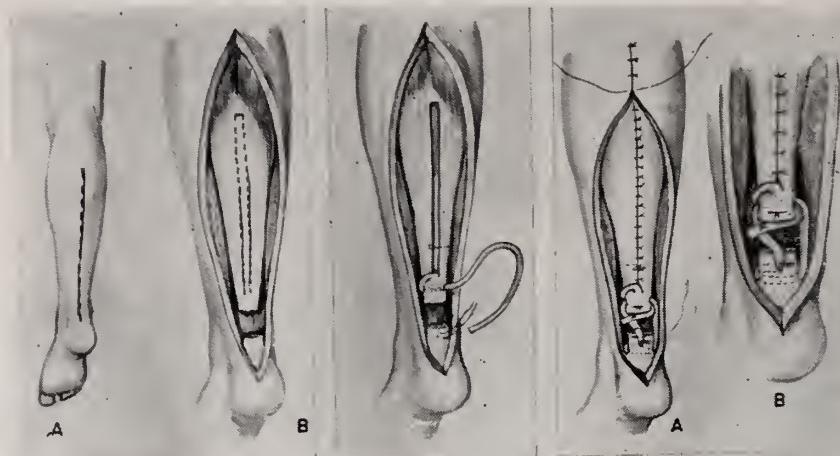


Figure 2  
Bosworth's technique for repair of rupture of Achilles tendon.

Immediate repair of fresh ruptures of the tendo Achillis with an end to end suture or Bunnell pull out wire suture offers excellent results. Delayed repair or repair of old ruptures is an entirely different problem. Repair of the defect by replacement with fibrous tissue is unsatisfactory, as the fibrous tissue stretches gradually and is unable to withstand the stress of the calf muscles. Spontaneous bridging of the gap by tendinous tissue following rupture uniformly fails to occur.

Several types of repairs using fascia lata, plantaris tendon, kangaroo tendon, and free tendon graft have been advocated, but the results are not entirely satisfactory.

In our cases we have followed a modification of the Bosworth's procedure. This consists in turning down a strip of tendon (buckle-

type fashion) from the proximal part of the raphe of the tendo Achillis to bridge the gap. This procedure was used in five cases. (Table I)

TABLE I - RUPTURE OF TENDO ACHILLIS

Case No.	Age	Date Injury	Mode Injury	Date Surgery	Surgical Findings	Result	Complications	Technique	Discharge
1	24	1952; Partial tear untreated	Playing baseball	3-5-56	2" tendon gap; fibrous tissue	Good	Wound dehiscence	Bosworth's	6-13-56
2	62	6-3-58	Laceration with a spade	9-26-58	3/4" gap	Fair; old fracture of ankle	0	Modified	1-23-59
3	23	6-5-58	Slipped on wet floor	11-8-58	1-1/2" gap; plantaris hypertrophy	Excellent	0	Modified	2-2-59
4	42	5-2-59-Sutured at City Hospital	Laceration with can	7-13-59	1" defect	Good	Wound infection	Modified	10-1-59
5	21	10-26-60	Machete wound	3-6-61	1-1/2" defect	Good	0	Modified	7-2-61
6	33	9-6-61	Playing basketball	9-7-61	Fraying of tissue	Excellent	0	Modified	12-1-61

### Material and Results:

All patients except one were young individuals. Five were males and one female. In two of them rupture was due to sudden contraction of the calf muscles and in three it was caused by sharp trauma.

The time of repair of the tendon averaged three to five months after the injury, in four cases; In one case, the repair was done four years after the injury. The site of rupture was located between 1" to 2" above the oscalcis. These cases have been followed for one to six years. In three cases, the calf muscles still show some atrophy. The range of motion of the ankle joint returned to normal in all. Hypertrophy of the repaired tendon has persisted in four cases.

The last (No. 6) case, although operated twelve hours after the injury is included in this report, because at the time of surgery the tendon ends were so shredded that an actual loss of length was present. The only logical way to repair the defect was using a tendon graft.

### CASE 6:

This 33-year old male sustained an injury to his leg while playing basket-ball. Examination three hours later revealed loss of plantar flexion of the foot, depression over the tendon, swelling and echymosis of calf muscle, non-reaction to squeeze test and loss

of push-off. Operation was performed 12 hours after the injury with the patient in the face-down position after applying a pneumatic tourniquet to the leg.

#### Operative Technique (Case 6):

The skin incision was started at the proximal third over the calf muscles curving at the distal third exposing the entire Achilles tendon and the tendinous raphe. (Fig. 3A) The sheath was filled with blood clots, the proximal end retracted and the tendon completely shredded at both ends. The ends were excised leaving a gap one and a quarter inches long. A half inch strip was cut and freed from the central portion of the raphe from above-downward and was left attached to the proximal end just above the defect. (Fig. 3B) The strip was passed through the full thickness of the proximal end of the tendon, pulled down posteriorly across the gap, inserted through a vent in the distal end, and brought upward and folded on itself. (Fig. 3 C, D). With the foot in slight plantar flexion, the folded strip was anchored with interrupted sutures. The defect in the raphe was approximated with interrupted cat-gut sutures. (Fig. 3E) A long leg plaster cast was applied with the knee in flexion and the foot in slight plantar flexion and the leg was immobilized for six weeks. Gradual weight bearing was then permitted for six weeks and full weight bearing in twelve weeks. Physiotherapy consisting of whirlpool, push up, and muscle strengthening exercises was given.

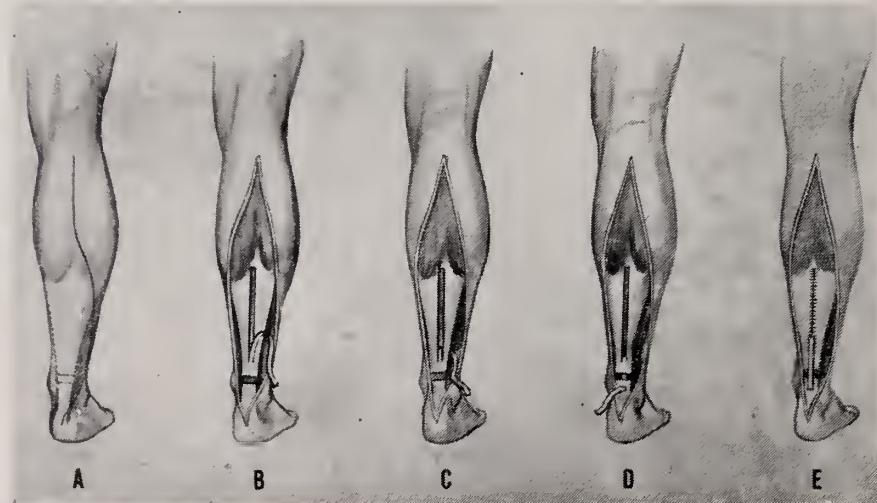


Figure 3  
Modified procedure for repair of tendon.

**Comment:**

This modified procedure for the repair of rupture of the Achilles tendons has been used only in five cases, but we feel it offers the following advantages: 1. As the skin incision is curved medially or laterally, it avoids crossing transverse scars from previous injury and there is less probability of wound dehiscence. 2. The simple folding of the tendinous strip in "buckle-type fashion" provides for more length and less chance of strangulation.

**SUMMARY**

A modification of the Bosworth's technique for the repair of rupture of the Achilles tendon is described. This procedure has been used successfully in five cases. It is recommended strongly for the treatment of delayed repair of ruptures of the tendon and in fresh ruptures where end to end apposition is not feasible.

**RESUMEN**

Se describe una modificación de la técnica de Bosworth para la reparación de roturas del tendón de Aquiles. Se ha usado con éxito el procedimiento en cinco casos. Se recomienda su uso en el tratamiento de casos de roturas viejas y en casos de roturas recientes cuando no es factible la aposición.

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## PSYCHIATRIC-SOCIAL STUDY OF A PREPAID MEDICAL PLAN\*

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The S S S (Seguros de Servicio de Salud de Puerto Rico) is a prepayment medical insurance plan. While it does not cover psychiatric treatment, it provides for psychiatric diagnosis. In practice, this is considered to be equivalent to one visit to the psychiatrist.

During the summer of 1962 the S S S was much in the news because it had encountered grave financial difficulties. These naturally gave rise to the question as to how the plan was being utilized. Doctors were heard to complain that the plan was being abused by patients; it was said that patients covered by the plan consulted the doctors for the merest trivialities. It was under these circumstances that the idea of the present study occurred to the author.

During the month of August 1962 seven S S S patients paid initial visits for consultation in the private office of the author. The latter in his role as psychiatrist was indeed struck by the casualness with which some of these seven came for consultation. The question nonetheless remained whether factors could be demonstrated which should differentiate these cases from patients not covered by the plan.

A comparative study was retrospectively made of these seven patients using as controls an equal number of private patients, i.e., patients not covered by the plan. The seven controls were secured from the psychiatrist's daybook according to the date of the initial visit of each an inverse chronological order from the end of August 1962. The entire fourteen cases were then scored plus or minus in regard to each of three criteria. These criteria were (1) whether the patient was referred to the psychiatrist by a physician, (2) whether he came for repeated visits, and (3) whether he had a history of previous psychotherapy. These criteria were considered meaningful in the context of the study because their presence corresponded to predictability and their absence to unpredictability or casualness. Thus it was considered that a patient referred by a doctor would be more likely to have a good reason for coming for consultation, other things being equal, than one not so referred. Likewise, a repetition of the visit spoke for a disturb-

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\* Presented at the Annual Convention of the Puerto Rico Medical Association November 17, 1962.

ance of relative gravity. Similarly, the history of previous psychotherapy made the present consultation with the psychiatrist more foreseeable in the patient's life pattern. The three factors chosen as criteria, then, indicated a degree of severity of the problem or a previously manifested disposition to make use of psychiatric services or both; in either case the presence of the enumerated factors was considered to have increased the probability or actuarial predictability that a given patient should present himself for psychiatric consultation. The absence of these factors, on the other hand, was regarded as having decreased the probability or actuarial predictability or, what amounts to the same thing, increased the casualness. (See Table I)

TABLE I

Patient	Referral by Physician	Re- peated Visit	Previous Treatment	Patient	Referral by Physician	Re- peated Visit	Previous Treatment
N. (f.)	+	+	+	R. (f.)	+	+	-
L. (m.)	+	-	-	Fl. (f.)	-	-	-
C. (f.)	+	+	-	P. (m.)	-	-	-
B. (f.)	-	+	-	G. (f.)	-	-	-
O. (m.)	+	+	-	M. (m.)	-	-	-
Ch. (f.)	-	-	-	V. (f.)	-	-	-
U. (f.)	?	+	+	Z. (f.)	-	-	-

Sex distribution is the same among the two groups, each consisting of five females and two males. Otherwise there is the most marked contrast. Four out of seven of the control group were referred by a physician; in addition, the case marked by the question mark had a previous acquaintance with the psychiatrist and previous treatment elsewhere so that she did not come "blind". In contrast, only one of the S S S cases was physician referred. Five out of seven of the control group required a repetition of the visit to the psychiatrist, whereas only one of the S S S cases did. Two of the control group had received previous psychotherapy, whereas none of the S S S had.

An additional factor, not included in the table, that struck the psychiatrist in relation to two of the SSS cases was the vagueness about the presentation of the problem. In these two cases it was not clear who was to be considered the patient. In one case where

a man was the nominal patient he came accompanied by his wife. Each complained about the other in such a manner that it was evident that the problem was marital and the couple were referred accordingly. In another case, the nominal patient was a young wife who came unaccompanied; however, her complaints centered about her husband who had to be sent for to clarify the situation. Among the control group, in contrast, in no case was there any doubt as to who was to be considered the patient.

It is observed from the table that in six of the seven SSS cases there were exclusively minuses in regard to the three criteria of comparison between this group and the controls. In only one of the seven of the control group was this pattern seen; the rest had one, two, or three plusses. The one SSS case that did not conform to the prevalent SSS pattern of three minuses had two plusses. The distribution within the SSS group and the private group of the three criteria or predictability factors shows that predictability in terms of these factors was significantly less among the SSS group than among the controls ( $p$  is less than .015).

In summation, SSS patients consulting a psychiatrist displayed an altered actuarial pattern from private cases; their incidence could not have been predicted on the basis of incidence of private patients. If analogous differences exist throughout the medical and surgical fields in general, the complaints of the physicians on the one hand and the financial difficulty of the SSS on the other become comprehensible. The characterization of the altered pattern as an abuse of the plan may represent the subjective reaction of some physicians and is understandable; whether it should not have been anticipated from a business standpoint is another question. One wonders whether it is fair to accuse patients of abuse when they attempt to make use of services which they consider themselves to have paid for in advance. One method of protecting the solvency of the plan in future might be to limit specialist services to those patients referred to the latter by the doctor treating them; there may be other methods. In any case, the altered pattern under the SSS is a fact, whatever name be put upon it.

## PHYSICIAN RESPONSIBILITY IN DISASTER PLANNING

*GEORGE W. PASCHAL, JR., M.D.*

All disaster planning must be predicated on the assumption of survival. This implies the survival, not only of the individual, but of the Nation. All planning must be based upon considerations of maximum catastrophe in any given disaster. In recent years as we have expanded our awareness of the enemy's destructive potential and have learned of our own unprecedented capacity to wreak destruction, our efforts have been directed toward planning to successfully provide for our population ways and means for survival. Much progress has been made in the past 15 years. There is yet much to be done. We should not defer action until stimulated by such a thing as a Cuban Crisis, or until we are hanging on the brink of disaster. The Federal Government and our State Governments are aware of the need for realistic planning and most are doing something about it. There are many facets to the over-all problem of Civil Defense. Those of the Medical-Health Group have a responsibility second to none of the others.

It is in this area that the physician comes into focus. It is in this area that the physician finds himself in a dual role. First, he had the role of individual physician, and secondly, he finds himself joined with his fellows to provide a broad service to the entire population which only Organized Medicine can provide.

Let us first consider the responsibility of the individual physician. It should be borne in mind that the physician is in a unique position of providing a service which he and only he can provide. In the United States there are less than 250,000 physicians to care for our 1800 million citizens. Today, in peace, most of these doctors are busily engaged in doing work from that of general practitioners, to that of highly trained specialists. From time to time a local plane crash, train wreck, earthquake, devastating fire, hurricane or a tornado disrupts a placid orderly existence to force upon these doctors the care of these unpredicted victims. The local physician usually rises to the occasion and meet the emergency with credit to himself and his profession. The physician's role in local disaster is, then, only an expansion of what he does every day such as treating hundreds at a school made ill by food poisoning, repairing seven severely wounded in a single auto accident, etc., etc.

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Professional competence is expected of the physician. The people he serves rely upon him for advice. The physician has the responsibility to prepare himself to properly inform his patients as to the dangers which could occur in disaster and the precautions to be taken in the event of it. The public and many doctors have been persuaded that there is no satisfactory resistance to the effects of thermonuclear warfare. This has lulled many into attitudes of defeatism. Here, the doctor as a physician, as a citizen, is in a position to use his influence to correct the misinformed. There are no better people than the individual members of the medical profession to explain these facts clearly, simply, calmly, tactfully to their patients so that they should know where not to worry and so that they should know when they should. Many of our physicians have acquired the attitude that if we have all-out attack with thermonuclear weapons that "the end is at hand." Survival is possible. All doctors should know that this is possible, even probable, with proper preparedness. The individual doctor has the right to his own opinion but he has no right to abrogate the responsibility to the people he serves. To effectively serve these people he has the responsibility to lend his talents toward preparedness, prevention, treatment, and rehabilitation. To do this calls for complete understanding of the problem which might be faced and how it might be met. Patients will rightfully look to their doctor for advice and how to prepare for the possible devastation about which they read, how to prevent harmful effects from the radiation to which they might be subjected, how to treat themselves if he —their doctor— is not available and what they may do afterwards. The people look to their doctors for their answers. They don't expect them to come from H.E.W. or D.O.D. It has been said that "the gift of intelligence which created society can destroy it." But I say to you that that same intelligence, properly used, can save it. I believe the individual physicians of this country will do their part.

The individual physician, joining with others forms a component, which when many are added together, builds the structure of organized medicine. It is this body which has the major responsibility in Disaster Planning. This is true because of the varied and complex services the Medical-Health Services have an obligation to provide for our Nation in time of emergency. To satisfactorily discharge the trust and responsibility it accepts without dispute calls for realistic planning, organization, education and training. It calls for rehearsing, repeated re-evaluation of plans and an unending effort toward preparedness which will afford our people a sense of security and make any aggressor aware of the futility of attempting to render our Nation to a state beyond

recovery. This, I believe, is our greatest contribution to Disaster Planning and to solid structure of our Civil Defense posture.

The Summary Report on National Emergency Medical Care is perhaps the most significant accomplishment of the American Medical Association directed toward the outlines of responsibility for the medical profession and of the physician himself. It embodies the cooperative efforts and expanded functions of our Allied Health Groups. This report which has appropriately been called "The Bible" of Disaster Medical Care outlines the responsibility of the medical profession, in respect to preparation for, and recovery from, a mass attack on the United States, to provide the leadership and guidance that will:

- a. Promote sound mass casualty planning at all levels of government and at all levels within the professional medical and health organizations.
- b. Encourage the population of the United States to engage in individual and collective survival training.
- c. Lend assurance that successful recovery from a mass attack is possible.
- d. Ensure adequate medical training of personnel of the medical and health professions and of all other personnel potentially able to assist themselves and the health professions in the care and treatment of the survivors of a mass attack.
- e. Ensure full utilization of available medical and health personnel resources, including selected segments of the general public, both prior and subsequent to a mass attack.
- f. Ensure proper steps to be taken so that optimum amounts of the required medical supplies and equipment are stockpiled and ready for use in the event of a mass attack.
- g. Ensure the development, through research, of improved and increasingly effective methods of preventing and treating disease and injury.
- h. Ensure prompt mobilization of all available necessary personnel for provision of the medical care that will be required subsequent to a mass attack.
- i. Ensure provision of the best possible medical care to the maximum number of casualties within the means available subsequent to a mass attack.
- j. Ensure prevention of unnecessary illness, injury and loss of life during and subsequent to a mass attack.
- k. Ensure maintenance of the health, physical stamina and morale of the uninjured survivors of a mass attack.

Disaster Planning requires long range considerations and in-

volves all segments of our Allied Health Groups in addition to physicians themselves. The full utilization of osteopaths, dentists, veterinarians, nurses, medical and dental technicians and technologists in all categories, medical, social, and psychiatric workers, hospital dietitians, ambulance drivers, hospital administrators, medical librarians, pharmacists and others should receive training to equip them to perform expanded functions under austere conditions or unusual emergencies. City, County and State Societies have the responsibility for the education of these Allied Health professions.

Organized medicine has traditionally met emergencies. They, in fact, have prepared for them. Preparation and training forms the broad base upon which the practice of medicine is established. The Clinician utilizes his fund of knowledge to cope with every day problems and from his understanding directs treatment with success. In Disaster Planning it is the duty of the Physician to again broaden his knowledge to fully comprehend the vastness of problems with which he may be faced. In time of extensive devastation and the production of mass casualties the American people will look to the American physician for help, advice, and comfort. With proper planning and preparedness medical men will get the job done.

Planning and training is slow business. A long range effort must be made. While there is yet much to do it is some comfort to reflect on what has been accomplished. Those of us familiar with the evolution of Disaster Medical Care can note the change and progress of the program as a whole. We look forward to a continuing, expanding process of training and preparation which not only is for physicians but for civilians as well.

The Physicians have available courses in Mass Casualty Care at certain Army Centers. State and County Medical Societies sponsor symposia and lectures within reach of all. The fact that Accrediting Agencies for Hospital Certification now require the presence of a Mass Casualty Plan and periodic tests and rehearsal of these plans has done much to bring this matter to local levels. While this affords preparation for local disasters it also becomes one of many nuclei which can merge with others in the event of a massive calamity.

Offering one of the brightest prospects for sound, successful training is the MEND — Medical Education for National Defense program. This has been expanded so that it now includes most all of our medical schools. Students, having received this training, demonstrated a capacity of leadership, resourcefullness and competency in helping provide care for the thousands displaced in a Texas hurricane. As succeeding classes acquire their

degrees and settle in varied communities, the task of planning and preparedness will be made the easier. We have an immediate responsibility for the impending danger of the day, but we look forward to the future with confidence that the medical profession will be trained to cope with disaster.

The U. S. Public Health Service with the guidance and co-operation of the American Medical Association has developed a Medical Self-Help training course. The success of this program will insure the training of large numbers of people capable of helping themselves as well as others. Since this program was inaugurated it has been accepted with enthusiasm throughout the country. Plans are being developed for it to be included in the curricula of our schools, not just for the time being but as a continuing educational process. Already thousands have successfully completed this course and many more eagerly await the opportunity to take it. The State and County Societies are actively supporting this endeavor. Even on quick reflection the observer can not but be impressed with the massive potential and capabilities of this segment of our population in providing care for our people under austere and disaster conditions. The nature of thermo-nuclear war demands that physicians have the special training necessary to insure the survival of the greatest number possible. The stark reality that the limited number of physicians available will not be able to render all of the services which will be necessary makes it even more urgent that the Medical Self-Help program be pushed with vigor.

It has been gratifying to observe the rapport between Public Health Departments and Committees of Disaster Medical Care. Certainly the problems of health and sanitation will be greatly increased. In the eventuality of mass attack the load of the Public Health Service would be taxed beyond capacity. Physicians would then be required to assume responsibilities in this field and be prepared to direct communicable disease control, food and water inspection, sanitation advice, personal and area hygiene and mass feeding supervision. A clear understanding regarding radioactive monitoring and its methods is imperative. The physician must accept expanded training and functions. The Medical-Health fields complement each other and both are inter-dependent on the other.

In every state a number of 200-bed Civil Defense Emergency Hospitals are prepositioned and stand ready for use in disaster. In my State, and I assume in all states, there has recently been concluded an inspection and updating of these hospitals, readying them for operational use if the necessity arises. Provisions for supplies for 30 days of functioning are being stocked. Larger storage areas are being found for those not adequate for continued

occupancy. Many of us are guilty of doing little or nothing about training and manning these hospitals. Since these facilities might well afford communities their only usable hospitals, it is of dire importance that staffing be planned, training be carried out, rehearsals and testing done, and preparedness be accomplished. To begin this sort of thing when it is actually needed is too late. We must act in this area of preparation while there yet is time.

Civil Defense and disaster management functions, at all levels of government, are designated by law. With few exceptions, the medical and health service is placed under the direction of the health officer. Respect for and cooperation with constituted authority is essential. The medical profession through its representatives seek the continued pleasant relationships and exchange of information and ideas with State officials which is of mutual interest and benefit to both. The medical profession is fully aware that it cannot meet a disaster of overwhelming proportions alone. It knows it must function under competent and informed leadership and under the law. It realizes its dependence of many other services such as communications, transportation, food, water, power, fuel, welfare, rescue, etc., etc. It —organized medicine—believes that our government and all of its associated agencies and services recognize their dependence on the service only we can provide. The realization of this enormous responsibility is enough to make us shudder. It should also stimulate us to renewed and continuing effort to discharge our obligations with credit to ourselves and our profession. To do this we shall survive, and what is more important, so shall our Nation.

## RADIODIAGNOSIS\*

HERIBERTO PAGAN SAEZ, M.D.

### Case Summary (No. 4-63):

This twelve year-old white female with the complaint of a bony growth in the left temporal region associated with severe headaches. There is no history of trauma to the head.

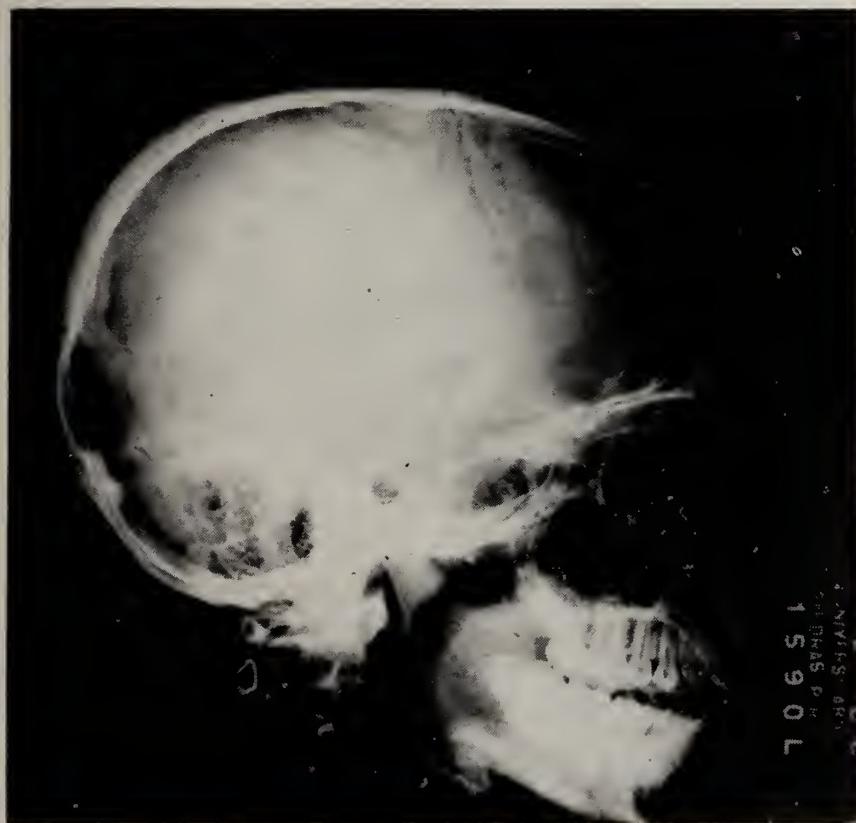


Fig. 4

\* From the Department of Radiology, School of Medicine, School of Tropical Medicine, University of Puerto Rico, Rio Piedras, Puerto Rico.

**Interpretation:**

There is evidence of an osteolytic irregular lesion with well defined sclerotic borders in the left temporo-parietal region. There is no evidence of lesional calcification.

**Diagnosis:**

Epidermoidoma

Epidermoidoma (Cholesteatoma) of the Calvarium. This tumor arises in the diploe of the calvarium, expanding both bony tables. It is due to an ectodermal cell rest. Cholesterol crystals are contained in the fibrous capsule of the tumor. The tumor is variable in size.

This lesion is not to be confused with the cholesteatoma found in the middle ear following chronic infection, which represents epithelial and fatty debris resulting from the admixture of ceruminous material with the epithelial and inflammatory debris of chronic infection of the mastoid antrum and middle ear.

## SECCION DE RESUMENES

**HYPERBILIRUBINAEMIA IN FULL-TERM NEWBORN INFANTS: A FOLLOW-UP STUDY** (Evolución de bebés hiperbilirrubinémicos nacidos a término), Killander, A., et al., Servicio de Pediatría del Hospital Universitario, Uppsala (Suecia), *Acta Paediatrica* 52: 5: 481 (Sept. 1963).

93 bebés hiperbilirrubinémicos, todos nacidos a término, ninguno con incompatibilidad Rh, fueron examinados a la edad promedio de 26 meses. De los 93, 46 recibieron exanguinotransfusión cuando su bilirrubinemia alcanzó la tasa de 20 mgs%; los 47 restantes salvaron ese escollo espontáneamente, sin que se les cambiara la sangre, a pesar de que todos también llegaron a alcanzar tal tasa sanguínea. En ninguno de los dos grupos pudo Killander reconocer signos de kernicterus y no hubo diferencias significativas en su desarrollo neurológico. Concluyen los autores que, cuando no existe enfermedad hemolítica, sólo debe cambiarse la sangre a aquellos bebés a término que presentan una hiperbilirrubinemia excesiva, o sea, superior a 25 mgs%.

MANUEL E. SOTO VIERA, M.D.

**USE OF FLUOXIMESTERONE IN THE TREATMENT OF GROWTH RETARDATION** (Empleo de la fluoximesterona en el tratamiento del retardo del crecimiento), Zvi Laron, Universidad de Tel-Aviv (Israel), *Acta paediatrica* 52: 5: 465 (Sept., 1963).

53 niños de ambos sexos —21 prepúberos y 32 en la pubertad, pero todos con edad ósea retardada— recibieron fluoximesterona diariamente por boca durante seis meses. Esta substancia, cuya acción miotrófica es dos veces más potente que su efecto androgénico, promovió tanto el crecimiento ponderal como estatural de los sujetos. Cree el autor, en discrepancia con otros, que la fluoximesterona estimula la maduración ósea, y que lo hace sin sacrificio del crecimiento lineal. No sabemos, sin embargo, cómo evitar (sin causar perjuicio a su acción anabólica, al darla por períodos más largos) sus efectos secundarios. La virilización que provoca aparece a una posología de 0.15 mgs/kg/día en el prepúber, y de 0.1 mg/kg/día en el adolescente.

MANUEL E. SOTO VIERA, M.D.

**SCHISTOSOME OVA; RAPID METHOD FOR BULK ISALATION FROM TISSUES OF INFECTED MICE** (Huevos de Schistosoma mansoni en Tejidos de Animales Infectados: Método Enzimático Rápido y Sencillo para su Separación a Granel). Toro-Goyco, E., Rivera-Collazo, E., and Rodríguez-Molina, R. *Science* 142: 407, 1963.

Se infectaron ratones con *Schistosoma mansoni* según el método de Ritchie. A las ocho semanas se sacrificaron y se les removió el hígado y el intestino. Estos tejidos fueron homogenizados usando un buffer de acetato a pH 4.0 como solvente en proporción de 2 ml. por cada gramo de tejido. Posteriormente se incubaron los homogenizados a 37° por tres horas añadiéndole la enzima proteolítica pinguináina (obtenida de la fruta de maya *Bromelia pinguin* L.) en proporción de 10 miligramos de enzima por cada gramo de tejido. Luego de la digestión los tejidos se filtraron por una red metálica de 100 orificios por pulgada cuadrada. Se añadieron ocho mililitros de solución salina al ocho por ciento a tubos de ensayo y a cada uno de ellos se añadió cuidadosamente, formando una capa sobre la solución salina, un volumen de 5 mililitros del filtrado. Centrifugados los tubos en una centrífuga de mesa por un minuto a

1,000 revoluciones por minuto, los huevos del parásito se hallaron depositados en número abundante al fondo de los tubos. La preparación de huevos así obtenida estaba libre de partículas de tejido animal. Los huevos obtenidos reaccionan positivamente a la prueba de circumoval.

E. TORO GOYCO, Ph.D.

**THE BINDING OF RADIOACTIVE TRIIODOTHYRONINE BY ERYTHROCYTES IN MYOCARDIAL INFARCTION** (La captación de triyodotironina radioactiva en los Eritrocitos en Infartos del Miocardio). Toro-Goyco, E., Ramírez, E. A., y Rivera, Julio V., con la asistencia técnica de Rivera, Eliseo. Am. J. Med. Sciences 245: 692, 1963.

La captación de triyodotironina radioactiva en los eritrocitos se encontró aumentada transitoriamente en 19 de 24 pacientes con infarto agudo de miocardio estudiados serialmente. Se encontró que esta elevación no guarda relación con la terapia de heparina o bishidroxycoumarina. La captación de  $T_3$  fué normal en siete pacientes con insuficiencia coronaria sin infarto, cinco pacientes en anticoagulantes por tromboflebitis aguda, uno con pericarditis y en veinte otros que recibieron terapia con bishidroxycoumarina crónicamente. En 22 casos de arritmias cardíacas de varios tipos, sólo 7 tuvieron una captación elevada, y éstos todos tenían o infarto del miocardio o enfermedad renal hepática avanzada.

J. L. CIANCHINI, M.D.

**THE BINDING OF RADIOACTIVE TRI-IODOTHYRONINE BY ERYTHROCYTES IN MYOCARDIAL INFARCTION** (Captación de tri-iodo-tironina por los eritrocitos en infarto del miocardio). Toro-Goyco, E., Ramírez, Eli; Rivera, Julio V., con la asistencia técnica de Rivera, Eliseo. Am. J. of Med. Sciences 245: 692, 1963.

En estudios seriados de 24 pacientes con infarto del miocardio, 19 de ellos demostraron durante la fase aguda un aumento transitorio en la captación eritrocítica de tri-iodo-tironina marcada con radioiodo.

No se encontró relación entre esta anomalía y el tratamiento con heparina o bishidroxycumarina (Dicumarol). La captación fue normal en siete pacientes con insuficiencia coronaria sin infarto, en cinco con terapia anticoagulante para tromboflebitis aguda, en uno con pericarditis y en veinte otros que por un periodo de tiempo prolongado venían recibiendo bishidroxycumarina. En 22 pacientes con arritmias cardíacas de varios tipos apareció aumentada la captación solo en siete, en los cuales también había infarto miocárdico o daño severo renal o hepático.

Se postula que como resultado de necrosis celular, el miocardio libera substancias desconocidas que alteran la avidez de los eritrocitos o las proteínas del plasma para la tri-iodotironina.

J. L. CIANCHINI-ANSELMI, M.D.

**HUMAN LIPOPROTEINS: ROLE IN THE TRANSPORT OF THYROID HORMONES** (Lipoproteínas Humanas: Su función en el transporte de hormonas del Tiroides). Toro-Goyco, E., Cancio, M., VA Hospital, San Juan, P. R., Science 139: 761, 1963.

Muestras de sangre de pacientes que habían recibido yodo radioactivo ( $I-131$ ) con fines terapéuticos fueron obtenidas 24 y 48 horas después de la dosis. El suero fue separado por centrifugación y el yodo inorgánico removido usando resinas de intercambio iónico.

Las lipoproteínas del plasma fueron aisladas por ultracentrifugación, usando para ello la técnica de gradiente de densidad. Se encontró que la fijación por las lipoproteínas de baja densidad de hormonas del tiroides, medidas como hormonas radioactivas, es insignificante. La fijación de dichas hormonas por las alfa lipoproteínas (lipoproteínas de alta densidad) es significativa. La mayor parte, sin embargo, se transporta fijada a proteínas de una densidad mayor de 1.23 gramos/mililitro, que obviamente no son lipoproteínas. Estos hallazgos están en conflicto con algunos hallazgos informados en literatura reciente.

E. TORO GOYCO, Ph.D.

— — —



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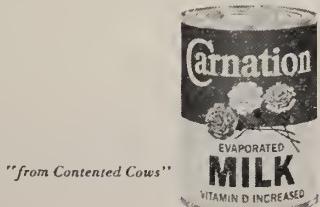
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El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudieran ser de interés general para la profesión médica.

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b) En página separada debe incluirse lo siguiente: título (no excediendo de 80 letras y espacios), nombre del autor(es), grados académicos, institución y dirección postal del autor.

c) Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: (1) introducción, (2) material y métodos, (3) resultados, (4) discusión, (5) resumen (en español e inglés), (6) referencias.

d) Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: (1) introducción, (2) observaciones del caso, (3) discusión, (4) resumen (en español e inglés) y (5) referencias.

e) Las tablas, notas al cálce y leyendas deben aparecer en hojas separadas.

f) Si un artículo ha sido leído en alguna reunión o conferencia debe así hacerse constar.

g) Deben usarse los nombres genéricos de los medicamentos. Pueden usarse también los nombres comerciales, entre paréntesis, si así se deseae.

h) Se usará con preferencia el sistema métrico de pesos y medidas.

i) Las fotografías y microfotografías se someterán como copias en papel de lustre sin montar. Los dibujos y gráficas deben prepararse a tinta negra y en papel blanco. Todas las ilustraciones deben estar numeradas (números árabigos) e indicar la parte superior de las mismas. Debe escribirse una leyenda para cada ilustración e indicarse en el texto donde debe ir colocada. Un máximo de 6 ilustraciones, por artículo, serán permitidas sin costo para el autor.

j) Las referencias deben ser numeradas sucesivamente de acuerdo con su aparición en el texto. Los siguientes ejemplos pueden servir de modelo:

6. Koppisch, E. Pathology of arteriosclerosis. Bol. Asoc. Med. P. Rico 46: 505, 1954. (artículo de revista)

4. Wintrobe, M. M. Clinical Hematology, 3rd Ed. Lea and Febiger, Philadelphia, 1952, p. 67. (libro)

Deben usarse solamente las abreviaturas indicadas en el Index Medicus, Biblioteca Nacional de Medicina.

Se podrán ordenar sobretiros del artículo cuando se reciba notificación de su aceptación.

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e) Tables, footnotes and legends to figures should appear in separate sheets.

f) If paper has been presented at a meeting the place and date of this should be stated.

g) Generic names of drugs should be used. Trade names may also be given in parenthesis if desired.

h) Metric units of measurements should be used preferentially. Abbreviations should be used sparingly.

i) Photographs and photomicrographs should be submitted as glossy prints, unmounted. Drawings and graphs should be made in black ink on white paper. All illustrations should be numbered (Arabic) and top indicated. A legend should be given for each and its location should be indicated in the text. A maximum of 6 illustrations is allowed without cost to the authors.

j) References should be numbered serially as they appear in the text. The following form will be used:

6. Koppisch, E. Pathology of arteriosclerosis. Bol. Asoc. Med. P. Rico 46: 505, 1954. (for journal articles)

4. Wintrobe, M. M. Clinical Hematology, 3rd Ed. Lea and Febiger, Philadelphia, 1952, p. 67. (for books)

Abbreviations will conform to those used in the Index Medicus, National Library of Medicine.

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**Dosage:** Adults, 1 teaspoonful every two or three hours. Children, six to twelve years:  $\frac{1}{2}$  teaspoonful every two or three hours. Do not exceed 7 doses daily. Administer to children under six years of age only on the direction of a physician, and do not exceed the recommended dosage.

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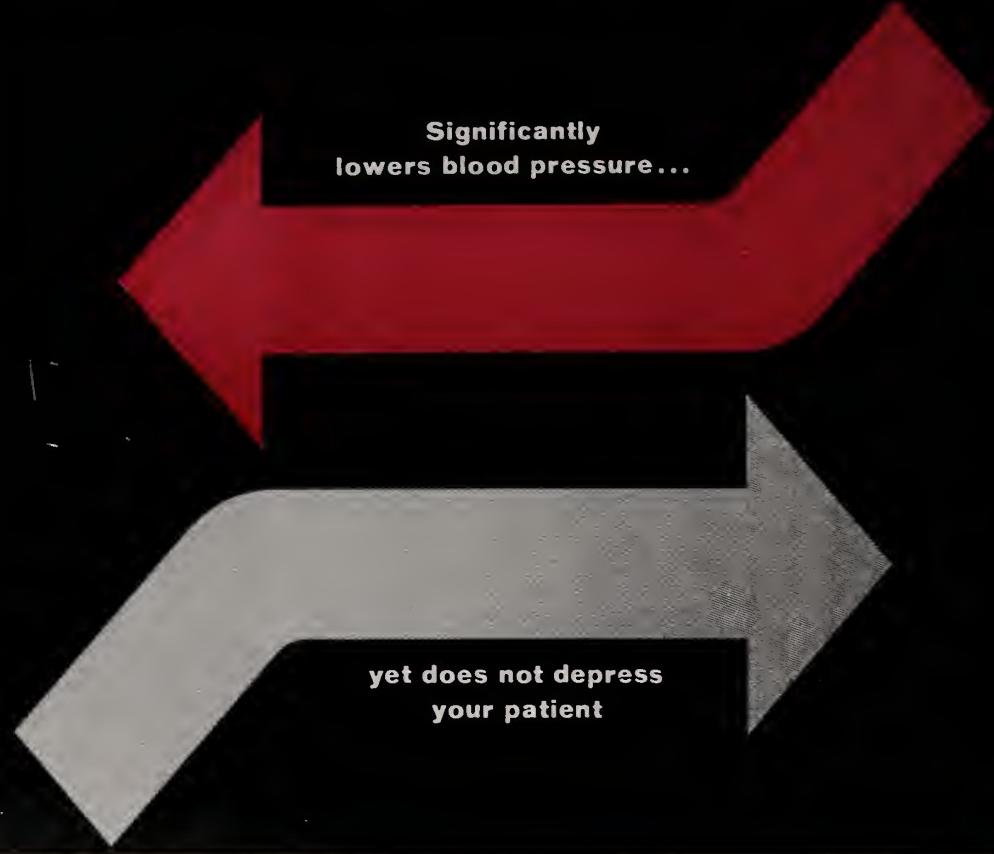
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This preparation may cause drowsiness. A patient should not drive or operate machinery while taking.

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Eutonyl is a unique member of a new nonhydrazine chemical series. Pharmacologically the drug is an MAO inhibitor. Yet, paradoxically, it acts to lower blood pressure. Results are definite, and often dra-

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No. This is a vital point of therapy. As you know, existing agents often will induce or aggravate depressive symptoms. Eutonyl will do neither. Indeed, many investigators have reported that patients often experience an increased sense of well being during Eutonyl therapy.

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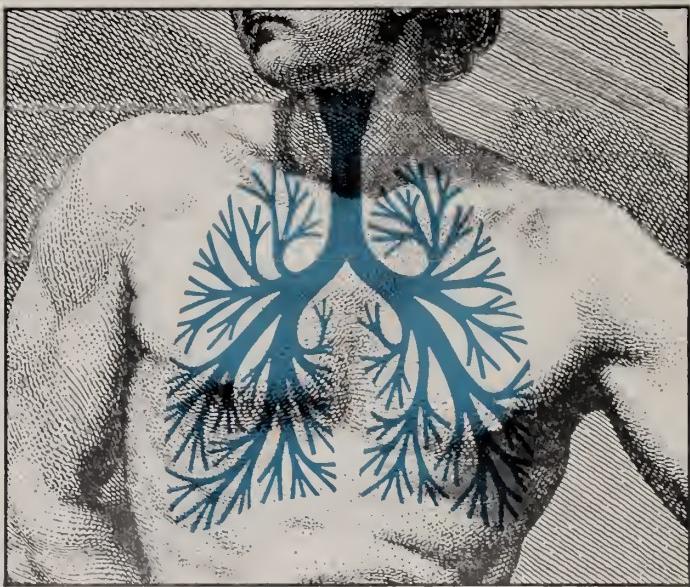
Yes. You may use Eutonyl alone or with other antihypertensive agents, including thiazides or thiazide-thiawolffia combinations. Or as replacement for other nondiuretic antihypertensives. In such cases the starting dosage may be reduced.

See your Abbott Representative for full details and literature; or write to Abbott Laboratories Puerto Rico, Inc.

\*Significant—Minimum 20 mm. Hg. reduction in mean blood pressure† and/or achievement of normotension.

†Mean Blood Pressure— $\frac{1}{2}$  pulse pressure plus diastolic pressure.





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For complete product details, consult Schering literature available from your Schering representative, or Medical Services Department, Schering Corporation, Union, New Jersey.

**Packaging:** Bottles of 30, 100, 1000. Tablets of 0.6 mg. each. \*TRADEMARK CE-S4G-J-PR

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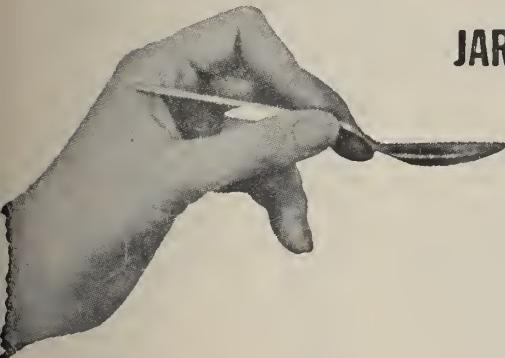
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**Precautions:** Anuria.

\*From clinical data on file at Lederle Laboratories. Posed by model.

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# BOLETIN

DE LA ASOCIACION MEDICA DE PUERTO RICO

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NO. 2

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## DEL ESPRUE EN PUERTO RICO: AYER Y HOY\*

RAFAEL RODRIGUEZ-MOLINA, M.D.

PRIMERA PARTE

BAILEY KELLY ASHFORD

Hombre e Investigador

Año 1932. Acabábamos de regresar de la Universidad Johns Hopkins luego de cursar estudios de parasitología médica, de salud pública y de estadística. Habíamos aprobado el año de residencia necesario para el doctorado en ciencias en esa Universidad. También nos habíamos entrenado en el Laboratorio de Maxwell Wintrobe para hacer morfología de la sangre. Con el hematocrito de Wintrobe esperábamos clasificar las anemias del esprue y de las parasitosis prevalecientes en Puerto Rico. Huelga decir que llegamos a casa con un entusiasmo y alegría propios de la juventud, agradecidos por la oportunidad que se nos había brindado para cursar estudios post-graduados en los Estados Unidos y con muchas ideas para encauzar un programa de investigaciones en un futuro inmediato. Una de las primeras personas con quienes hablé en la Escuela de Medicina Tropical fué el Dr. Ashford. Puse a su consideración los estudios que planeábamos hacer en relación al esprue, la esquistosomiasis y la uncinariasis.

Por aquel entonces las autoridades del Hospital y de la Escuela hicieronme cargo de los pacientes de esprue en el dispensario y los ingresados al hospital. Desde entonces y hasta el verano de 1934, el Dr. Ashford y yo nos veríamos con frecuencia en la Escuela o en el hospital. Yo solía informarle de artículos recientes que aparecían en diversas revistas médicas y él los comentaba. Para esa época ya el doctor se sentía enfermo y no asistía regularmente a su oficina de la escuela.

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\* Conferencia ofrecida en tributo a la memoria del Dr. Bailey K. Ashford (1873-1934), pronunciada en el anfiteatro de la Escuela de Medicina el día 4 de noviembre de 1963, a las 8:30 P.M.

Tenía yo que hacer recuentos de glóbulos rojos y determinaciones de hemoglobina dos veces por semana a cada paciente. Una noche, estando de guardia me encontraba en el pequeño laboratorio clínico en el segundo piso del hospital, haciendo un cómputo de glóbulos rojos para un paciente de esprue, me avisaron que el Dr. Ashford deseaba vernie. Estaba el doctor platicando en el pasillo del segundo piso con unos señores y al verme dijo: "Excuse me a minute, I will be right over with you". Al poco rato sentí una mano sobre la espalda y era el Dr. Ashford que deseaba hablar conmigo. "Listen here, where did you learn to do a blood count? — Your results in this patient do not correctly indicate the amount of anemia he has. I want you to show me right away just how you go about to perform a red blood count and a hemoglobin determination." Entramos en el laboratorio y dos horas más tarde aún estaba allí el Dr. Ashford observándome cuidadosamente y pendiente del más mínimo detalle mientras yo le demostraba cómo hacer un cómputo de glóbulos rojos. Nada más se dijo sobre el asunto y nunca volvió a llamarme la atención sobre los resultados obtenidos en pacientes anemizados.

Verano de 1934. Ya el Dr. Ashford se encontraba postrado y no asistía a su oficina de la escuela. Yo iba a verle de vez en cuando y me recibía en un saloncito detrás de su oficina y contiguo a un pequeño cuarto de exámenes en su residencia en el Condado, que da a la Avenida que hoy lleva su nombre — Ave. Dr. Ashford. Su aspecto daba lástima. Emaciado, pálido, notábbase muy decaído. Pero su voz aún indicaba una mente clara y alerta. A veces cuando yo llegaba lo encontraba dormitando y al verme decía: "Sit down Rodríguez, chat with me a while. What are the latest reports on sprue, on hookworm?" Yo empezaba a hablar pero de pronto él interrumpía diciendo: "This terrible pain in my back is killing me, the arthritis." Otras veces, cuando había recibido alguna inyección para calmar el dolor, mostrábbase decidor, casi eufórico, y con voz fuerte pero pausada, explicaba con entusiasmo y emoción su última teoría sobre la fase larval de la uncinariasis. Una tarde mientras hablábamos se presentó María, la fiel servidora de muchos años, para anunciar que allí estaba un paciente, un antiguo cliente del doctor que deseaba verlo. Esa tarde vestía el doctor la toga con el fez a la cabeza que usara en ocasión, según decía él, cuando le confirieron el Doctorado Honoris Causa en Medicina de la Universidad del Cairo en Egipto, honor que le fuera otorgado en el año 1924, en ocasión de la celebración en esa ciudad de un Congreso Internacional de Medicina Tropical.

Al ser informado que un paciente estaba esperándole, el doctor trató de levantarse del sofá en que estaba acostado. Yo le ayudé a incorporarse y me dijo: "I want to see and examine that

patient." A duras penas podía caminar, aquel hombre débil, escuálido y enfermo. Yo le sostenía lo mejor que podía, agarrándole por los brazos y por los hombros. Con capa y con fez a la cabeza entramos al cuarto de examen. El paciente era un viejecito con esprue de muchos años y estaba sentado sobre la mesa de examen a medio vestir. Al vernos no pareció sorprenderse, y mientras yo agarraba al maestro por ambos brazos, éste, con el estetoscopio auscultaba el corazón y los pulmones del paciente. Nunca podré olvidar esta escena sombría y conmovedora. ¡Cuál no sería la fe que aquel viejecito tenía en su médico, en el hombre que abatido y víctima de un mal crónico e incurable, le estaba examinando casi sin poder tenerse en pie! Y sin embargo, la fe y la confianza que el paciente tenía en su médico no había mermado.

Encontrándome en Nueva York en el otoño de ese mismo año una mañana leí en el "New York Times" la reseña de la muerte y de los funerales del Dr. Ashford. El pueblo de Puerto Rico le había tributado un homenaje digno del amor y de la admiración que sentía por él.

En el año 1950 bajo el título "Background for a Medical School in Puerto Rico", discurso pronunciado por el que os habla en un banquete ofrecido por el "American College of Physicians" decíamos en parte lo que sigue:

"The Puerto Rican mountaineer or "Jíbaro", the agricultural laborer of the hills who led a sickly, pauperized and miserable way of life, was at the turn of the century the subject of sociological and medical interest and the concern of the land-owners. He had been described as indolent, apathetic, and lazy by the men of letters of that generation.

In 1899, a terrific hurricane struck the island of Puerto Rico disrupting its agriculture and much of its economic structure. A young and well trained medical officer in the United States Army was assigned to set-up and operate a field hospital for civilians, to treat the homeless and destitute peons and their families, victims of the storm. During the course of the daily routine of his work, it occurred to this curious physician, that in addition to examination of the blood of these pale and sickly people which he had carried out and confirmed the well known fact that they were anemic, he should perform examination of the stools. It was a hot afternoon, when Lt. Ashford in his small, improvised laboratory at the foot of the hills, in the city of Ponce, examined the feces of one of his patients. Suddenly, he saw under the microscope the eggs or ova of the deadly hookworm. Rejoicing with excitement and enthusiasm he immediately sent his Commanding Officer at San Juan, the following telegram: "Ponce, P. R., November 24, 1899. Have this date proven the cause of many pernicious pro-

gressive anemias of this Island to be due to *ancylostomum duodenale*". The veil had been lifted from the face of the anemia of Puerto Rico. This discovery constituted a cornerstone of research in the field of medical science in tropical areas. In the course of the next several years it was followed by the introduction of mass treatment, that is, the administration of an anthelmintic drug by medical personnel to a large number of people in a given area and in a given period of time. "The anemia campaign", as it was called, was carried out in several parts of the island with monies appropriated by the Government of Puerto Rico, and under the supervision of the Porto Rico Anemia Commission. It was the first campaign against this disease in the new world and over 300,000 persons were to be treated in the course of the following five years. It was this type of therapy which in later years the International Health Board of the Rockefeller Foundation was to carry out over the tropical world with the purpose to erradicate and control parasitic diseases, particularly malaria and *ancylostomiasis*. — Dr. Ashford's discovery of the pathogenesis of the anemia affecting thousands of agricultural laborers in Puerto Rico and elsewhere, has, in our opinion, no less significance and consequence in terms of human suffering and in lives saved, than the experiments of Walter Reed, and his associates in yellow fever in the city of Havana. Death from "the anemia" had fallen from 11,875 in the years 1900-1901 to 1,738 in the years 1907-1908. At about this time two other important discoveries took place: The finding by Dr. Isaac González-Martínez of the ova or eggs of *Schistosoma mansoni* in native Puerto Ricans marked the discovery of this important parasitic disease in the western hemisphere. As early as 1908, Dr. Ashford described the clinical syndrome of sprue on this island. While the struggle against the hookworm was being carried out all over the rural areas of Puerto Rico, it was felt by influential men in the government that an official institution was desirable and necessary to direct the crusade against this disease and at the same time to study other medical problems which had already appeared in connection with the hookworm program.

The Institute of Tropical Medicine and Hygiene was inaugurated at San Juan in the year 1912 with Dr. Bailey K. Ashford as the first Director.

Following the 1st World War in which Colonel Ashford actively participated with an outstanding record of service, and during which he became in contact with many of the leading medical men of his generation, the idea of a bigger institution, a place where graduate medical education, as well as research on a larger range would and could be carried out, became paramount in the mind of

Puerto Ricans and Continentals in high government positions, and particularly in the mind of Dr. Ashford.

In a new and beautiful building the School of Tropical Medicine was inaugurated in the year 1926, and the institution was to function as a semi-autonomous part of the University of Puerto Rico under the auspices of Columbia University. The aims of the post-graduate school were the study of disease in a semi-tropical environment, research, teaching, and above all, service to the people of Puerto Rico and to the Medical profession of the Island. I will mention but a few activities of the School of Tropical Medicine. The clinico-pathological conferences, the visits of distinguished men in medical science, the availability of scholarships for post-graduate education abroad. Today such activities are of frequent occurrence, but in those days they were practically non-existent for the benefit and advancement of the medical profession of Puerto Rico. In this connection, the present Commissioner of Health had said: "Many of us, particularly those who came, as I did, during the early years of our School of Tropical Medicine, can well remember the tremendous influence that this institution had on medical practice in those days". Twenty four years later we can point out to the service rendered by the School of Tropical Medicine to the people of Puerto Rico, through the treatment of thousands of indigent patients in the dispensary and in the hospital; to the medical profession, and among other services, the rendering free of charge of pathological examinations on surgical material; to the hospitals in the metropolitan area for performing free autopsy service; to the Department of Justice of the Government of Puerto Rico in preparing medico-legal work on certain autopsied material. In addition, and to mention just a few, there are its medical library with over 14,000 bound volumes and nearly 500 periodicals; the research on nutrition as it concerned the diet of Puerto Ricans; the investigation on the pathogenesis of recurrent lymphangitis; the epidemiological, pathological and clinical studies on schistosomiasis mansoni; the studies on chromoblastomycosis and the pathology and epidemiology of filariasis. Such is, ladies and gentlemen, the spiritual, the scientific heritage and the tradition of the Porto Rico Anemia Commission, of the Institute of the Tropical Medicine and Hygiene, and of the School of Tropical Medicine. They are great underlying forces and efforts which will exert their influence in the life of the new Medical School. The men and women who incarnated these three sources of new life for medical science in Puerto Rico are not to be forgotten. With such a background, which we trust will not be forsaken or ignored, but should always be had in mind, we firmly believe

that the new institution has been established on a permanent and lasting foundation.

It is a difficult, complex and time consuming task to set-up a medical school. The local members of the American College of Physicians are fully cognizant and appreciative of this fact. In their name and in my own, I wish to express our greetings, our admiration and our respect to those responsible for the creation of the Medical School, for their leadership, for their devotion, and for their courage to carry out their ideals of public service."

#### LAUDEMUS VICOS GLORIOSOS

On December 16, of the year 1933, the School of Tropical Medicine at San Juan, P. R., was the scene of a ceremony which placed a historical landmark in that institution, and which took place in honor of Puerto Rico's most eminent citizen — Dr. Bailey Kelly Ashford.

A bronze bust of the illustrious scientist, a work of indubitably high artistic merit by Margorie Daingerfield Holmes was unveiled and presented to the School of Tropical Medicine by the Acting Governor, in the name of the Governor, the Legislature, and the people of Puerto Rico.

In a short speech of acceptance the Director of the School, Dr. George W. Bachman said:

"This morning we are gathered together to honor a beloved colleague and a renowned citizen of Puerto Rico.

"Others will speak of his life, labors and accomplishments—no words of mine could add to the prestige of him, whom we all know, esteem and love. He himself has founded his own fame solidly and independently upon the rock of life and service given for others.

"Today we symbolize that fame by the bestowal of this bronze statue upon a grateful people, placing it in the School of Tropical Medicine which he has unselfishly and abundantly served.

"To our immediate association it will be a silent and ever present inspiration of courage and victory in the face of often overwhelming odds: To the people of Puerto Rico who have made possible this noble gift, it is a visual recognition of the affection felt by rich and poor alike for one who has given his services freely and impartially—not only do they regard him as a healer, but as an instructor who has indicated the way of health to thousands living in hookworm infected areas; to future generations, it will be pointed to with pride as a symbolized standard of high achievement by which to measure their own attainments.

"This bust is the best means we have of recording the man

His scientific work, his literary achievements are poor substitutes for his glowing personality.—Not even years dedicated to strenuous scientific research could detract from the symmetry of this beautiful rounded character, wrought graciously from life as this bust has been wrought from sterling metal.

“Mr. Chairman, in the name of the Special Board of Trustees and the Faculty and staff of the School of Tropical Medicine, I wish to thank the Governor of Puerto Rico, Acting Governor Horton, the Legislative Assembly, and the people of Puerto Rico for this worthy gift, and accept it with gratitude dedicating it to future generations.”

Y ahora, señoras y señores, para terminar la primera parte de esta conferencia deseo leerles unas estrofas del poeta — que considero caracterizan al hombre cuya memoria honramos aquí esta noche. De José Santos Chocano, poeta de América, citamos los últimos versos de su poema “La Elegía del Organo”:

—¿ Por quién doblan ?

¿ Por quién doblan y se quejan y suplican las campanas ? —

Una flauta lo pregunta y otra flauta lo contesta :

—Por un hombre que fué herrero, fué soldado, fué poeta . . .  
¡ y eso basta !

Por un hombre que tenía tres estrellas en el alma :

el trabajo, la energía y el ensueño ;

el trabajo que da fuerzas, la energía que da audacias  
y el ensueño que da glorias :

¡ las tres gotas de la Sangre ! ¡ los tres sellos de la Herencia !  
¡ los tres gritos de la Raza !

Suena el órgano ,

suena el órgano en la iglesia solitaria ,

suena el órgano en el fondo de la noche ;

y hay un chorro de sonidos melodiosos en sus flautas . . .

## SEGUNDA PARTE

### AYER Y HOY

Iniciamos la segunda parte de la conferencia con una explicación de lo que nos proponemos hacer. Revisaremos a grandes rasgos la literatura regional sobre esta enfermedad que tanto se ha estudiado en nuestro país. En el ayer consideramos aquellos trabajos publicados después de la muerte del Dr. Ashford (acaecida en el año 1934), hasta la segunda guerra mundial. En el hoy incluimos aquellas publicaciones que salieron a la luz desde el 1947 hasta el 1963. Si el tiempo lo permite mencionaremos algunas investiga-

ciones del **ahora**, y luego diremos algunas palabras sobre el **mañana**.

De unos diez trabajos publicados desde el 1935 al 1943 escogemos dos que consideramos de particular interés e importancia por el número de pacientes estudiados y por el extenso enfoque del material clínico observado.

El trabajo "Revisión del Esprue. Estudio clínico y hematológicos de 150 casos", — por el Dr. Ramón M. Suárez, publicado en el año 1938<sup>1</sup> es una monografía completa de la enfermedad, en la que se estudian el diagnóstico clínico del esprue, incluyendo sexo y edad, y raza, contenido de sales de calcio en la sangre, sistema circulatorio, análisis del jugo gástrico, metabolismo, tubo gastrointestinal, hematograma, médula ósea del esternón y tratamiento por dieta apropiada y administración de extracto de hígado.

#### Conclusiones del autor:

1. Según hemos podido comprobar, existe indudablemente una predisposición racial y probablemente un factor hereditario predisponente en la enfermedad. 121 enfermos eran blancos, 26 mulatos y sólo 3 pertenecían a la raza negra. Varones: 82, hembras: 68.

2. Las alteraciones óseas, observadas por los investigadores europeos y norteamericanos, no han podido comprobarse en esta investigación.

3. Hay una baja de metabolismo basal, según fué observada en 10 casos estudiados.

4. Como éste es un país tropical donde abundan los estados diarreicos, la prueba de la tolerancia de la glucosa tiene, en nuestra opinión, cierto valor para formular el pronóstico de la enfermedad, pero esta misma prueba no es tan importante en Puerto Rico para formular el diagnóstico de esprue.

5. El dato de laboratorio más constante en todos los análisis practicados es la presencia de una anemia macrocítica, generalmente de tipo hipercrómico, alguna vez hipocrómico, con una pulpa medular de tipo megaloblástico.

6. El autor propende a considerar el esprue como una enfermedad que se origina principalmente en el sistema hematopoyético, y no en el tracto gastrointestinal.

A pesar de su escaso contenido de vitamina B<sub>12</sub> el extracto concentrado de hígado dió resultado muy beneficioso en el tratamiento del esprue tropical aún en los casos que existían complicaciones de la médula espinal.

8. La mortalidad por esprue en la isla de Puerto Rico se calcula en 65 por millón de habitantes durante el año.

En el 1943 se publica el trabajo "El Esprue en Puerto Rico.

Resultados en 100 casos de esprue al cabo de diez años", por R. Rodríguez-Molina.<sup>2</sup> Citamos:

"En comunicaciones anteriores hemos estudiado la sangre periférica y el aspecto del hematograma y el cuadro clínico en cien sujetos de ambos sexos que sufrían del esprue libre de complicaciones. En esta comunicación presentamos los mismos cien casos, cuyo curso posterior con el resultado del tratamiento instituido, hemos observado durante diez años, guiándonos como propósito principal el poder apreciar el estado de salud de un grupo de casos consecutivos que habiendo recibido un tratamiento semejante al final de un período determinado de tiempo, nos permitiese determinar la historia clínica del síndrome esprue tropical tal como se presenta en Puerto Rico.

Cuando el síndrome del esprue se ha establecido plenamente constituye una enfermedad crónica por carencia, que se caracteriza por su comienzo insidioso y sintomatología crónica, con trastornos gastrointestinales de desarrollo progresivo, consistentes principalmente en una dispepsia,\* inflamación y descamación de la lengua y la boca, meteorismo intestinal y diarrea. Las deposiciones suelen ser líquidas, espumosas, de color grisiento, pestilentes, frecuentemente de gran volumen y abundantes en grasa. La estomatitis, la gastritis atrófica y la rectosigmoiditis suelen ser las manifestaciones más importantes. En el 90 por ciento de los casos suele existir una anemia de tipo macrocítico o hipercrómico con aspecto megaloblástico de la médula ósea. La pérdida rápida de peso y corpulencia se da en los enfermos en la misma proporción y la fiebre en 40 por ciento.

Esta sintomatología puede desarrollarse y alcanzar su apogeo en el curso de varias semanas, o más generalmente, en pocos meses. Como lo típico de la sintomatología es su cronicidad, este complejo sintomático puede durar, si no se trata, varios años, antes que sobrevenga la muerte. Los relapsos son cosa frecuente, pero la remisión de los síntomas gastrointestinales o de la anemia es, por lo que hemos podido observar, muy rara.

La pérdida rápida de peso y energías suele ir acompañada de hipermotilidad intestinal, deficiente absorción alimenticia y finalmente un estado caquéctico progresivo y crónico. La perturbación del metabolismo de las grasas, de los hidratos de carbono y de los proteídos son causa de que se altere la absorción intestinal, y según se cree, ello tiene una relación esencial con el cuadro sindrómico.

El grupo de sujetos que hemos estudiado se componía de cin-

\* Con el término "dispepsia" comprendemos la siguiente sintomatología: Distensión abdominal, repleción o incomodidad epigástrica, ardor de estómago y dolor después de las comidas.

cuentiún varones y cuarentinueve hembras, cuyas edades fluctuaban entre doce y setentiocho años, con un promedio en todo el grupo de 40.14 años. El enfermo de más edad era un anciano de setentiocho años y el más joven una muchacha de doce años. Entre el grupo había ochentisiete blancos y trece de raza de color, dos de estos negros puros, y el resto mulatos. Todos los casos fueron observados en los dispensarios del Hospital de la Universidad (73) y en las salas del mismo (27). Los casos dados de alta en la sala seguían concurriendo después a los dispensarios. Según nuestros datos, noventiocho sujetos eran naturales del país, descendientes de españoles o mezclados con raza negra; los dos restantes, uno era un mulato venezolano, y el otro, un natural de los Estados Unidos que había vivido en Puerto Rico varios años antes de contraer la enfermedad. Excepto algunos pocos enfermos, todos pertenecían a los casos pobres e indigentes que, en el momento de ser examinados por primera vez, presentaban el cuadro clínico típico de esprue tropical en pleno desarrollo.

El extracto hepático en inyección intramuscular empleado en el tratamiento de estos casos se preparó de acuerdo con las instrucciones que nos fueron suministradas por el Dr. W. B. Castle el año 1931. Usamos el extracto crudo sin concentrar de la casa Lilly (Liver Powder Lilly, No. 343), pero su eficacia en el esprue y otras anemias macrocíticas pudimos comprobarla en nuestro Hospital y en otros de la localidad.

La dieta prescrita a los enfermos hospitalizados, y siempre que fué posible a los ambulatorios, es la misma descrita por el Dr. Ashford. En principio esta dieta contiene pocos residuos, gran cantidad de proteídos, poca grasa e hidratos de carbono, para facilitar así la asimilación y absorción de los alimentos ingeridos en presencia de la diarrea. No obstante, esta dieta contenía ciertos productos hidrocarbonados que se producen en el país, tales como plátanos verdes, bananos, yautías (tubérculo semejante a la patata), los cuales, sin que supiéramos por qué, parecen ser bastante bien tolerados y absorbidos por los enfermos de esprue. El objeto de la dieta es eliminar el exceso de hidratos de carbono (sobre todo el arroz y las habichuelas) y las grasas que suelen abundar en el menú ordinario de los puertorriqueños, sustituyéndolo por carnes, huevos, leche, verduras frescas y frutas. No creemos necesario incluir aquí con todo detalle los diferentes menús con que componíamos la dieta, los cuales convenientemente combinados, pueden suministrar al paciente unas 1,500 a 2,000 calorías diarias. La preparación más corriente de estos alimentos consiste en hervirlos y asarlos, sin usar apenas grasa y sólo alguna pequeña cantidad de mantequilla para condimentar las carnes, los huevos y los vegeta-

les. Los condimentos y las bebidas alcohólicas fueron completamente eliminados de la dieta.

El estudio que antecede demostró que setenticinco del grupo de enfermos de esprue sometidos a observación, después de darles de alta como curados, en el curso de diez años, ninguno ha retornado a la consulta. Trece casos están todavía bajo tratamiento y doce lo han abandonado, sin que sepamos el curso ulterior de su enfermedad. Entre los dados de alta mejorados, sesenta han continuado bien por espacio de cinco años, y por lo visto, no han sufrido hasta ahora ninguna recaída.

Con setenticinco enfermos dados de alta mejorados y sesenta curados, según todas las apariencias, por espacio de cinco años tenemos que pensar que el pronóstico del esprue es benigno, y depende mayormente de la edad del enfermo. El de los enfermos de menos de cuarenta años de edad es decididamente bueno; pero no así en los sujetos cuya edad se acerca a los cincuenta, no importe el sexo o la raza a que pertenezcan. Por grave que sea la sintomatología, cuanto más joven sea el enfermo más probabilidades tiene de curarse rápida y totalmente, siempre que se instituya oportunamente y de manera continuada el tratamiento apropiado.

Los resultados obtenidos demuestran la eficacia de la hepatoterapia, aunque no debemos olvidar que este grupo de enfermos se compone de sujetos pertenecientes a las clases pobres, muchos de los cuales no podían ser inyectados con regularidad ni ceñirse a la dieta alimenticia prescrita en el esprue. Estos factores indudablemente tienen cierta influencia sobre la duración del tratamiento, que suele durar, por término medio, unos tres años (oscilando entre un mes y diez años). El extracto hepático, además, no solamente prolonga la vida de estos enfermos; les devuelve la salud y la capacidad para las ocupaciones habituales. Antes de que se utilizase el extracto de hígado en el tratamiento del esprue, el promedio de vida de estos enfermos se calculaba en Puerto Rico en unos dos años. Así pues, la duración total de la vida parece haberse alargado, según se demuestra en este trabajo. A más de eso, como el estado de postración que acompaña a la anemia y la diarrea del esprue, limitaba la capacidad de trabajo de los enfermos, es evidente que la prolongación de la vida va seguida de un aumento de la actividad física que dura un número de años. Creemos que la vida probable de un enfermo de esprue tropical, sometido a un tratamiento adecuado, es poco más o menos, igual a la de los sujetos normales del mismo grupo de edad.

Más de la mitad de los enfermos fueron observados por primera vez en el año 1933. El número de enfermos ese año tiene cierta significación, por ser varias veces mayor que lo observado en los demás años que hemos empleado en este estudio. Ello, según he-

mos indicado, puede tener una gran relación con el desastroso estado económico-social y las consecuentes condiciones antisalubrarias que se dieron en este país a raíz de los ciclones ocurridos en el año 1932. La deficiencia alimenticia que entonces se produjo en nuestra población, fue el factor que más debió influir sobre el mayor número de casos acaecidos unos meses más tarde.

Créese que todos los síntomas del esprue obedecen a la medicación con el extracto hepático, no obstante lo cual se dan casos en que la administración hay que continuarla por espacio de meses y años. Con todo, si se quiere evitar las recaídas, hay que prescribir una dieta apropiada en la mayoría de los casos, si bien es cierto que, conforme los enfermos van sintiéndose libres de los síntomas gastrointestinales, puede permitírseles el uso de hidratos de carbono en su menú ordinario, evitando siempre, a todo costo, la ingestión de grasas y dulces.

En el 1947 aparece el primer estudio sobre la acción del ácido fólico en el esprue, por el Dr. Ramón M. Suárez.<sup>3</sup> Desde esa fecha hasta el 1953 este investigador publica diez trabajos acerca del efecto y eficacia del ácido fólico y la vitamina B<sub>12</sub> en el esprue tropical. Dichos trabajos, en algunos de los cuales colaboran el Dr. Tom Spies y otros investigadores puertorriqueños, constituyen piedra angular en el tratamiento moderno del esprue. La eficacia de esta vitamina quedó plenamente demostrada. La ingestión diaria de 10 mgs. es suficiente para lograr una marcada mejoría de los síntomas clínicos y la anemia. La dosis de sostenimiento es de 5 mgs. diarios. Demostró el Dr. Suárez que una dosis de 20 mgs. asociada a una dieta adecuada produjo mejores resultados que igual dosis acompañada de dieta indecuada.

Desde octubre de 1953 un grupo de jóvenes y preparados investigadores del cuerpo médico del ejército de los Estados Unidos ha estado trabajando en el "Tropical Research Medical Laboratory" de San Juan, interesados en el problema de la mala-absorción del esprue. Los nombres de Gardner, Hightower, Butterworth, Nadel, son bien conocidos. A ellos se unieron los investigadores puertorriqueños Enrique Pérez-Santiago, Calixto Romero, Martínez de Jesús y Santini.

Por qué el ejército de los Estados Unidos habría de realizar un programa a largo alcance y enviar aquí varios investigadores para estudiar el problema del esprue en nuestro país, cuando lo cierto era que con el extracto de hígado, el ácido fólico, la vitamina B<sub>12</sub>, y por otras razones, la incidencia del esprue había disminuido en Puerto Rico. —Porque el ejército deseaba estudiar la función del intestino delgado, pensando que tal estudio podría explicar el porqué de la rápida e intensa pérdida de peso que el Coronel William Stone había observado en los heridos de la guerra de Korea.

El ejército consideró a nuestro esprue como una enfermedad prototípico del intestino delgado, con el objeto de estudiar la función de esa víscera, a la luz de las técnicas modernas.

Conviene aclarar que tanto Ashford, como Suárez y Rodríguez-Molina, observaron un esprue que se caracterizaba por la presencia de síntomas intestinales, la presencia e intensidad de una anemia tipo megaloblástico, que se determinó en más de 90 por ciento de los enfermos. En otras partes del mundo ese tipo de anemia se había señalado en el esprue pero la incidencia no era tan alta como en Puerto Rico. El cuerpo médico del ejército de los Estados Unidos deseaba averiguar si el esprue puertorriqueño era la misma enfermedad que se observaba en Hong Kong y en la India. Los investigadores puertorriqueños interesados en la hematología habían presentado al esprue como una enfermedad predominantemente hematológica.

Con la presencia de un nuevo grupo de investigadores el estudio del esprue se tornó más intenso. Así pues el Dr. Ramón Suárez continuó sus estudios sobre el tratamiento, el Dr. Angel Cintrón-Rivera, de la Escuela de Medicina, y el Hospital de la Capital, inició un estudio de las anemias megaloblásticas de Puerto Rico. El Dr. Conrado F. Asenjo se une al grupo del Hospital de Veteranos para continuar y extender un estudio de la absorción de grasas. Las conferencias internacionales sobre el esprue celebradas cada dos años por el "Tropical Research Laboratory", han traído a Puerto Rico autoridades como Chester Jones, Frazer, Culver, Grey, Turner, Wintrobe y otros. Estas conferencias han brindado la oportunidad de repasar los resultados obtenidos y de hacer planes para futuras investigaciones. Hasta el presente se han celebrado siete de ellas, la primera en el año 1955 y la última en el 1962. Se espera que la próxima se lleve a cabo en el 1964.

Repasaremos ahora los trabajos que a nuestro juicio tienen más importancia y significación, realizados por el grupo de investigadores del ejército. No ha sido tarea fácil escoger los más sobresalientes de unos cincuenta temas diferentes.

En el 1956 Frank Gardner<sup>4</sup> publica un estudio sobre "El Síndrome de malabsorción en individuos en el servicio militar en Puerto Rico". Se observa pérdida de peso, diarrea, dispepsia y debilidad — pero ninguno de los 21 casos estudiados tuvo anemia. Pruebas de laboratorio demostraron absorción pobre de glucosa, D-Xylose, Vitamina A y grasa. La mayoría de los pacientes mejoró con el ácido fólico. Seis casos eran puertorriqueños y los restantes norteamericanos. Añade el autor que el diagnóstico del esprue en Puerto Rico quedó comprobado por los estudios de Suárez y de Rodríguez-Molina.

Pérez Santiago y Butterworth Jr., en el 1957<sup>5</sup> publican un tra-

bajo con el título de "Definición y diagnóstico del Esprue". Se estudiaron 79 pacientes de esprue con el propósito de relacionar la clínica con las pruebas de mala-absorción intestinal. Se observó que las pruebas de la "xylosa" y de la grasa en la excreta fueron anormales en el 95% de los casos. La absorción de Vitamina A fue baja en el 85 por ciento de los pacientes. El 90% de los sujetos dió resultados anormales en dos o más pruebas. Opinan los autores que además de la sintomatología clínica (la diarrea, glositis, médula megaloblástica), la presencia de malabsorción deberá demostrarse por lo menos por dos pruebas con el propósito de fijar o comprobar el diagnóstico del esprue.

A continuación comentaremos sobre unos cuatro trabajos que acerca del tema "Cambios patológicos en la mucosa del yeyuno en pacientes de esprue" publicados por los doctores Butterworth, Pérez-Santiago, Crosby, Smith y Kluger, desde el 1957 al 1960.<sup>6,7,8,9</sup> Se sabía que sí había atrofia de la mucosa intestinal en el esprue, pero que era producida por cambios sucedidos después de la muerte. Koppish<sup>10</sup> en el 1947 había observado a la autopsia cambios anormales en las velocidades de la mucosa intestinal, además de atrofia del corazón, bazo, hígado y lengua. Pero ahora los actuales autores al remover un pedacito de la mucosa intestinal con un delicado instrumento, observan lesiones estructurales en el paciente vivo que padece de esprue. Estos hallazgos confirman que había lesiones estructurales de la pared intestinal, que sin lugar a dudas podían observarse bajo el lente de microscopio. Los estudios de la biopsia del intestino delgado en pacientes no tratados y tratados es tan trascendental como lo es el uso del ácido fólico en el esprue por el Dr. Suárez y Spies y sus asociados en la década 1947-1957.

Para terminar con los trabajos del "team" de los chicos del ejército tan solo mencionaremos dos a la ligera. "Absorción Oral de las Pruebas de Tolerancia en el Esprue", por Frank Gardner y Enrique Pérez-Santiago,<sup>11</sup> Pruebas de tolerancia utilizando "xylose", mantequilla y Vitamina A, se hicieron antes y durante el tratamiento de un grupo de pacientes de esprue. Se observa absorción pobre antes del tratamiento. A pesar de que todos los pacientes mejoran con tratamiento de ácido fólico y Vitamina B<sub>12</sub>, las pruebas de absorción no mejoraron. La persistente mal-absorción indica que la mejoría en el defecto o estado de carencia hemático-nutricional no está asociado necesariamente a la mejoría en el defecto intestinal de mala-absorción. Los resultados indican que el esprue de Puerto Rico no es una deficiencia nutricional reversible.

Los resultados obtenidos por Butterworth, Pérez-Santiago, Martínez de Jesús y Rafael Santini<sup>12</sup> en sus estudios sobre la ad-

ministración oral y parenteral de la D-xylose en sujetos normales y en casos de esprue, demostraron concluyentemente la eficacia del uso de esta prueba en los estudios de mala-absorción.

Dejemos el grupo del "Tropical Medical Research Laboratory" y pasemos a la Escuela de Medicina Tropical. La determinación de grasa en las heces de pacientes de esprue era asunto que se conocía bien poco. No se había estudiado en Puerto Rico y casi nada se había hecho en el extranjero. No es agradable trabajar con deposiciones fecales en casos de esprue, particularmente cuando el paciente excreta una cantidad anormal de grasas, condición conocida por esteatorrea. Es la esteatorrea una de las típicas y constantes anormalidades que se observan en el esprue. Un sujeto sano que ingiere hasta 150 gramos de grasa en la dieta diarios, la cantidad de grasa en las heces no excederá de 6 gramos al día, esto es, cada 24 horas. Cuando la cantidad de grasa en la dieta sobrepasa de 200 gms. al día, habrá un exceso de grasas en la excreta, una esteatorrea fisiológica. Cuando la dieta es baja en ácidos grasos saturados y la ingestión de grasa diaria fluctúa entre 40 y 150 gramos, la excreción de grasas en las heces, y el porcentaje de absorción son constantes en el adulto sano. Tampoco se había estudiado los ácidos grasos presentes en las heces del paciente de esprue. Tenía que ser un bioquímico el que iniciara tales estudios en Puerto Rico, y fue así que el Dr. Conrado F. Asenjo publica en el 1952,<sup>13</sup> sus resultados sobre absorción de grasas en sujetos normales y en pacientes de esprue en nuestra isla.

Se determinó el por ciento de grasa en las heces secas en 41 pacientes de esprue y 19 sujetos sanos. Tan sólo el 29% de los casos de esprue y el 5% de los testigos excretaron más de 30 por ciento de grasa en las heces secas.

En otro grupo, 7 casos de esprue y 7 sujetos sanos se determinó el por ciento de grasa en las heces secas y el por ciento de absorción intestinal. La cantidad promedio de grasa en la excreta indicó que 2 de 7 casos de esprue tenían esteatorrea. Por otro lado el por ciento de absorción señaló que 5 de los 7 pacientes presentaban absorción anormal de grasa.

La excreción diaria de grasa en los pacientes de esprue tuvo un promedio de 12.5 gramos, indicando esteatorrea. En ninguno de los 7 testigos la cantidad diaria en las heces sobrepasó de 4 gramos.

Cinco años habrían de transcurrir desde este importante trabajo y la continuación y ampliación de tales estudios en el Hospital San Patricio para Veteranos, con la colaboración de los doctores Rodríguez-Molina, Marta Cancio y de las dietistas Matilde Dávila de Bonilla, Ada Montalvo de Irizarry y Gladys Torres de Muñoz.

Con el título de "Esteatorrea en el Esprue Tropical en Puerto Rico", publican un trabajo en 1957 Rodríguez-Molina, Asenjo y Cancio.<sup>14</sup> Indican los autores que el estudio se verificó por dos razones. Primero: por lo poco que se había escrito sobre el asunto; Segundo: porque el investigador inglés, Woodruff, había dicho —que el esprue observado en el área del Caribe, esto es, Cuba y Puerto Rico, no era como la enfermedad que existía en la India, pero sí más bien una anemia nutricional megalobástica asociada a síntomas gastrointestinales, pero no necesariamente a la esteatorrea — y por tanto a la malabsorción.

Para determinar la presencia e intensidad de esteatorrea en un paciente de esprue es necesario administrar una dieta diaria que contenga una cantidad fija de grasa fácil de digerir, además de otros alimentos — y luego determinar la cantidad diaria (cada 24 horas) de grasa en las heces. Esta prueba se conoce por balance de grasa. Se da al paciente una dieta contenido 80-100 gramos de grasa por un período de 8 días consecutivos. Al tercer día en adelante se recoge toda la excreta diaria (cada 24 horas) para determinar químicamente la grasa total en forma de ácidos grasos, tanto en la dieta como en la excreta. La experiencia nos ha enseñado que con esta dieta podemos determinar si un sujeto tiene o no esteatorrea, o sea, más de 6 gramos al día en las heces por cada 24 horas. Sujetos normales estudiados no excretaron más de 3 gramos diarios, aún cuando ingerían hasta 130 gramos de grasa diarios.

Estudios de balance de grasa se realizaron en 12 casos de esprue y 2 testigos. En 10 de los 12 pacientes se observó esteatorrea que fluctuó entre 8 y 50 gramos de grasa diarios.

En el 1958 aparece otro trabajo por Asenjo, Rodríguez-Molina, Cancio y Bernabe,<sup>15</sup> titulado: "Resultado de dieta muy baja en grasa con y sin gluten, en la excreción de grasa endógena en pacientes de esprue tropical."

Concluyen los autores que los enfermos observados muestran esteatorrea de origen exógeno, como resultado de una falla en la absorción de grasas, y no a causa de un aumento en la excreción de grasa endógena. Cuando los enfermos tomaron dieta baja en grasa (menos de 10 gramos diarios), la excreción de grasa endógena fué igual a la de sujetos sanos.

También se comprobó que considerando las condiciones del experimento el gluten de trigo no tuvo acción sobre la excreción de grasa endógena en los pacientes observados.

Hace varios años habíamos notado que algunos pacientes de esprue tratados con ácido fólico o con Vitamina B<sub>12</sub>, necesitaban además, dieta baja en grasa, pues de lo contrario se quejaban de distensión, gases y de diarrea, cuando comían más pan o bizcocho.

de lo corriente, y más grasa de lo acostumbrado. Y así fue que en el año 1960 Rodríguez-Molina, Cancio y Asenjo,<sup>16</sup> informan un estudio acerca de la acción del ácido fólico en la esteatorrea del esprue tropical y en otras pruebas de absorción intestinal.

Estudios de balance de grasa efectuáronse en 10 pacientes de esprue antes y mientras ingerían 15 mgs. de ácido fólico diarios por un período de 9 a 44 días y promedio de 23 días. Se observó esteatorrea en todos los pacientes antes del tratamiento. Otras pruebas de absorción tales como la excreción de Xylosa en la orina, la tolerancia de glucosa y la absorción de Vitamina A se hicieron antes y después del tratamiento con ácido fólico. La esteatorrea bajó considerablemente en dos pacientes y aumentó en otros dos bajo el tratamiento. En los ocho casos restantes no se observó gran cambio en esteatorrea. Las otras pruebas de absorción no mejoraron. A pesar de estos resultados todos los pacientes mejoran en su estado general, de la glositis, aumentaron de peso. Los valores hemáticos también mejoraron.

Dos años más tarde en 1962 los doctores Sheehy, Baggs y Pérez-Santiago<sup>17</sup> con el título, "Pronóstico del Esprue Tropical, estudio de la acción del ácido fólico sobre la fase intestinal del esprue agudo y crónico", observan 46 casos de esprue tratados con ácido fólico por dos o tres años. Concluyen los autores que el ácido fólico mejora rápidamente la condición clínica, pero no mejora la función intestinal, ni sana las lesiones del yeyuno con la misma rapidez. De uno a tres años transcurrieron antes de que las lesiones intestinales sanaran. Los autores estudiaron minuciosamente la mucosa intestinal antes y después del tratamiento.

En el año 1962 los doctores Julio V. Rivera y E. Toro-Goyco,<sup>18</sup> del Hospital para Veteranos, publican su trabajo sobre "La prueba de absorción de Trioleína en el diagnóstico de la esteatorrea". Se empleó la trioleína marcada con iodo radioactivo en sujetos sanos y en pacientes de esprue. Se obtuvo buena correlación entre la prueba de balance de grasa (método químico) y la prueba de iodo-trioleína cuando se determinó la radioactividad en las heces fecales.

El último trabajo que revisamos esta noche trata del gluten y el esprue tropical por los doctores Cancio, Rodríguez-Molina y Asenjo.<sup>19</sup>

Es bien conocido el efecto desfavorable que tiene el trigo en la enfermedad celiaca de los niños y en el esprue no tropical, condiciones similares al esprue de nuestro ambiente. Recordarán que estos investigadores habían estudiado la acción de una dieta baja en grasa y alta en gluten de trigo sobre la excreción de grasa en 9 pacientes, administrada durante 12 días, al cabo de los cuales se dió dieta baja en grasa y libre de gluten durante 12 días adiciona-

les. Durante un período de 24 días la grasa fecal se mantuvo en niveles normales.

En el presente estudio se empleó dieta libre de gluten por un período más largo, desde 12 a 33 días. Cuatro de nueve pacientes mejoraron marcadamente de su esteatorrea, otro enfermo mejoró notablemente luego de varios meses de haber seguido un régimen de restricción de gluten en su hogar. Clínicamente todos los enfermos mejoraron aunque los valores hemáticos mantuvieron más o menos iguales. La excreción de "xylose" en la orina aumentó en algunos pacientes.

Nos preguntamos ahora: ¿Acaso ha cambiado el esprue del ayer al hoy? No, el esprue no ha cambiado del ayer al hoy. —Ciertamente es que ahora muchos de los enfermos que acuden al médico presentan menos síntomas que antes: glositis sin diarrea, o diarrea sin glositis. Pérdida de peso sin diarrea y a veces glositis, diarrea, pérdida de peso pero ausencia de anemia marcada. Las facilidades médicas, las condiciones económico-sociales han mejorado rotablemente y los pacientes indigentes acuden al médico en un estado menos avanzado de la enfermedad que hace 30 años, observándose el mal al lado izquierdo del spectrum, por así decirlo.

Lo que sí ha cambiado son los métodos empleados para estudiar los enfermos — función del progreso, y de la evolución rápida y dinámica de la ciencia médica, que auxiliada, por la física y la química ha avanzado a pasos agigantados desde la terminación de la segunda guerra mundial. El desarrollo de nuevas técnicas e instrumentos de precisión crea nuevas oportunidades de investigación.

Creíamos ayer que el esprue era principalmente una anemia megaloblástica resultado de un estado carencial. Opinamos hoy que aún cuando se sabe que la anemia se debe a deficiencia de ácido fólico y Vitamina B<sub>12</sub>, la falla principal parece estar localizada en el intestino delgado, cuyos cambios anatomo-patológicos son causa aparente de la malabsorción de los alimentos.

Las presentes investigaciones de Rodríguez-Molina, Cancio y Asenjo sobre la acción del gluten, esto es, si la ingestión de esta sustancia produce recaída de la enfermedad, dará luz sobre el papel del gluten como factor etiológico. Los estudios epidemiológicos de Cintrón-Rivera y sus asociados en familiares de pacientes de esprue, indigentes y pudientes, nos dirán si la enfermedad es causada por carencia de substancias alimenticias en la dieta, o si es de origen familiar, hereditario, como creía el Dr. Ramón M. Suárez.

Y en cuanto al mañana — Los jóvenes médicos y científicos del ejército de los Estados Unidos y el grupo brillante, preparado y trabajador de nuestra escuela de medicina, continuarán sin lugar

a dudas, la lucha, la curiosidad, por conocer más y más a fondo esta enfermedad tan interesante, descubierta en América hace más de 200 años y descrita y trabajada en este país hace ya más de 50 años por el hombre e investigador cuya memoria recordamos aquí esta noche.

¿Cuáles son los mecanismos del tránsito intestinal de los alimentos en el intestino delgado y en el grueso? — ¿Cuánto tiempo tomarán las grasas, las proteínas, los hidratos de carbono y los electrolitos en pasar por el lumen intestinal? — He aquí problemas para estudiar, para atacar y resolver en el mañana.

Y ahora, señoras y señores, para terminar—los que hemos andado por el largo camino de la vida, llegamos a un punto de la vista en nuestras investigaciones, en que, emulando el añaño refrán castellano “Camino viejo y sendero nuevo”, hemos decidido encazar nuestras energías, un tanto cansadas y gastadas, por el sendero más reciente, limpio de zarzas y maleza — el de la esquistosomiasis experimental — y dejar que otros se abran camino — por el camino más trillado, más frecuentado y más sabido — y mejor, del esprue tropical.

Muchas gracias por la atención prestada.

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## A GROUP WORK EXPERIENCE FOR MOTHERS OF ADOLESCENTS WITH EPILEPSY

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Numerous recent publications have described the prejudices, misunderstandings and misconceptions concerning epilepsy widely held in the United States and elsewhere.<sup>1,2,3,4,5,6</sup> Epileptics are regarded with suspicion and fear; many people still believe that the epileptic is insane or cursed by the devil.

Parents of epileptics are not always free of these prejudices and misconceptions despite the fact that the epileptic's parents have had contacts with physicians. Livingston<sup>5</sup> of Johns Hopkins Hospital has pointed out that the parent's attitude toward the disease, the work in which the physician can gain cooperation and confidence of the parents, and the advice the physician can give to the parents to allow the child to lead as normal a life as possible are all crucial for the successful social management of epileptic children.

It has also been recognized that emotional problems act as precipitants to seizures in some patients. If the psychological environment of the epileptic's home is one of fear, tension, and prejudice, the successful management and rehabilitation of the epileptic become more difficult. As Yahraes<sup>7</sup> pointed out: "There are cases in which emotional tension brings on seizures. For these patients the doctor needs to find out not only the medicine which controls the seizures, but also the psychological treatment which will relieve the mind."

There is a need for consistent and organized educational programs for parents of children with epilepsy. The limited information usually given to parents of epileptics during brief office calls is not sufficient.

A pilot investigation which included a multiple therapeutic approach for the treatment of epileptic adolescents was completed recently. The treatment approach consisted of three phases: the utilization of pharmacotherapy, group psychotherapy for adolescent epileptics, and group work with the mothers of the adolescent epileptics. This report, describing for the most part the first dozen sessions of the group, is concerned only with the third phase of the research project, group work with mothers of adolescents with epilepsy. This phase of the treatment program had two major

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purposes: 1) to correct the prejudices and misunderstandings of group of parents of adolescent epileptics concerning epilepsy, 2) to reduce the anxiety and tension in parents.

#### METHOD OF STUDY

Two methods were used to study the progress of the program: participant observation and the recording of these observations; and the use of an attitude test. A transcript of the group's major transactions was prepared by the group leader after each meeting.

This transcript included the major concepts discussed, the attitudes and biases expressed by mothers and their emotional social behavior in the group. During several sessions an observer sat with the group and took extensive notes on the group's transactions.

The parents of 10 adolescents girls with epilepsy were invited to participate in this group experience. Concommitantly each of the epileptics was being treated with pharmacotherapy and some were in psychotherapeutic groups participating in the multiple treatment program. Despite an invitation to both parents, only the mothers attended the meetings. The mothers varied in age from 35 to 49 years. Their educational backgrounds were diverse: two were college graduates, three had attended high school, one had had no formal education and was illiterate.

Each mother was asked to complete a 50-item Attitudes Toward Epilepsy Test. This test was developed in order to determine objectively the parents prejudices, misconceptions and beliefs concerning the disease. The attitude test was based upon actual statements which had been made by the parents of epileptics in the past. The test was pretested in this section before its use. The mothers were asked to read each statement and to indicate whether or not they agreed with the statement. The following are some of the items which appeared on the test: "To have an epileptic child is a disgrace to the family." "Epilepsy is caused by heart trouble". "Epilepsy can be cured easily by spiritualism." "Epileptics are cursed." "Most epileptics are stupid." "Epileptics are queer and strange." "Epilepsy is God's curse on the parents." "Epileptics have special powers." "Epileptics are mysterious persons." "Epileptics are crazy." Table 1 shows some of the major items of the test with which 50 per cent or more of the mothers agreed. It should be noted that each of the respondents is a parent of a diagnosed epileptic and that each mother has had repeated contacts with physicians in the district hospitals of the island. Also it should be indicated again that some of these mothers were fairly well educated. Despite these facts, almost all of the mothers tested

agreed with many of the prejudiced, stereotyped misconceptions presented in the attitude test.

#### THE COUNSELING PROGRAM

The counseling program began formally in February, 1962 and has continued to this date. The mothers meet twice a month for a one-hour informal roundtable discussion. The group leader of all sessions has been this section's social worker. Below is a summary of some of the most significant interpersonal transactions which occurred during these group meetings.

The first session was devoted to the formation of the group and to the explanation of the program's purpose. All mothers accepted the idea and promised to participate regularly. At the end of the first meeting the mothers suggested the following topics be discussed in the forthcoming meetings: Epilepsy versus mental disease; different attitudes of parents toward epilepsy; and, epilepsy and marriage.

The second and third meetings were devoted primarily to the above topics. Of great interest was the fact that several mothers considered epilepsy a mental disease and that their own children were mentally insane. One mother suggested the group give itself the name, "Mothers of Epileptics Club." This proposal made a greater impact on the group. One mother denied that her daughter was an epileptic; several others objected strenuously and indicated that their daughters would feel very inferior.

The major concerns expressed by these mothers in the first three sessions were their terror and pain when an attack occurred, the inability of public school teachers to handle their daughters when an attack occurred in school, their shame and disgrace that one of their offspring was an epileptic, and their suffering because they were mothers of epileptics. The mothers were particularly fearful of sending their daughters to school. They expressed the worry that their daughter might have attacks on the street or on the road. Some considered their daughters defenseless and hence in need of constant supervision and protection. Three mothers indicated that they were afraid of some man's attacking their daughters after a convulsion.

In these sessions much information was obtained concerning the mothers' method of handling their daughters. Several indicated that they "protected" their daughters by hiding the fact that the daughter was an epileptic from friends, neighbors, and even from relatives. Some commented that one could only give more love, more security, and understanding to the child while others argued that the epileptic can only be managed through the use of consistent and firm discipline.

Four to six group sessions were devoted primarily to giving the mothers objective, factual information concerning the causes of epilepsy and the principles and methods of treatment of the disease. A physician from this section gave an informal lecture to the group on the background of the functioning of the human brain and upon the cause of epilepsy. The mothers asked questions and discussed the concepts presented by the physician's lecture. An educational film on epilepsy was shown which brought out more misconceptions the mothers had about epilepsy. Several mothers indicated that one could get epilepsy through the saliva of an epileptic and that the disease was highly contagious. These discussions taught the mothers that the epileptic "howl" is caused by lack of respiration during the attacks, that the frequency of seizures is related to menstruation and high anxiety, and that drugs can control the attacks. One mother indicated she would now insist that her daughter take her medication regularly and that she, the mother, would no longer go to "spiritualists" and "religious miracle workers" in the hope of obtaining a complete cure for her daughter.

By the end of the sixth session it became clear that several of the mothers developed resistance to the program. This matter was discussed in detail by the group and the following appeared to be the major reasons:

1. Two members were dissatisfied because they were sure that their daughters were not epileptics. Despite the presentation of objective, expert evidence, their denials continued.

2. The illiterate mother felt too timid and embarrassed to participate frequently in the group. She assumed that any question she may have had was silly due to her lack of schooling and would be considered by the other group members as a demonstration of her ignorance.

3. Almost all members of the group admitted that learning about their daughter's disease was a very painful process. Many had hoped simply to avoid the truth. Several cried upon learning that a complete cure in most instances was impossible at present.

Two group sessions were then devoted to improving and handling the mothers' resistances. The project psychologist attended these sessions and afterwards discussed the resistances with the group leader and the psychotherapist of the adolescents' psychotherapeutic group.

The attitude test toward epilepsy was repeated during the ninth group session. The results were compared with those of the first. The results were gratifying. Only two of the mothers indicated that they still adhered to their previous misconceptions. However, it should be recognized that intellectual acceptance is not

the same as emotional acceptance. By the ninth session, one mother still insisted that her daughter was not an epileptic. This comment prompted one of the others to declare that "some of us need help more than our daughters."

The tenth and eleventh sessions of the group were devoted to the discussion of their daughters' future plans. Most interesting in this discussion was the fact that every mother expressed the idea of letting her daughter decide what she herself wanted to do. This was a rather startling reversal of opinion since in the early group sessions each mother had described how the daughters must be protected, even overprotected.

It was also during the tenth and eleventh sessions that mothers mentioned spontaneously how these sessions had made them feel better. One mother put it this way, "It is easier to be the mother of an epileptic when you know there are other mothers who have the same problems you have." The mothers also mentioned that now that they understood their daughters' illness better, it was much easier to handle them. It was apparent that some of these mothers in fact did feel much more at ease in their relations with their daughters.

The twelfth session marked a major turning point in the activities and focusing of the group. The mothers had shown much concern about the lack of knowledge, prejudices and fears about epilepsy held by the general population of Puerto Rico. The mothers had repeated continuously that most Puerto Ricans reject epileptics and felt much fear and hostility toward persons with this disease. The mothers wanted to know if they could do something about this community problem. After much discussion the group decided to work toward the creation of a Puerto Rico Epileptic Parents Club. The proposed aim of the club would be to help educate the Puerto Rican public, and to aid doctors, parents and patients to solve the social and psychological problems of epilepsy. Subsequently the Club has been organized and its work has begun.

#### SUMMARY

The need for enlightenment on the subject of epilepsy in Puerto Rico is great. Few health problems are so incrusted with such an accumulated mass of prejudice, ignorance and misinformation. Even the mothers of epileptics, as the results from this study show, are not free from these prejudices despite the fact that many have had repeated contacts with physicians.

The major purpose of this report was to describe the group process employed in helping the mothers of 10 adolescents with

epilepsy. This process was part of a three phase program aimed at treating these patients. The mothers met in an informal group setting with a social worker on a semi monthly basis. The purposes of this program were to overcome the mothers' misinformation concerning the disease and to reduce their fears and anxieties.

Each mother was given an attitudes test on two occasions in order to obtain an objective measure of attitude changes which may have occurred. Each session was recorded by the group leader.

Nine of the ten mothers seemed to have changed greatly in terms of their attitudes and feeling about the disease. One mother, despite the same 10 months of participation in the group, still insists that her daughter is not an epileptic.

The mothers of epileptics were able through the group sessions to overcome many of their misconceptions and fears about epilepsy. We believe, on the basis of testimonials given by these mothers, that the adolescents with epilepsy have benefitted from their mothers reduction of tension and anxiety. In 9 to 10 cases, it would appear that these group sessions have led to a general reduction of tension within the home. The best medical care is of little avail, in our opinion, if the epileptic is exposed continually to a psychologically detrimental home environment.

TABLE I  
ITEMS FROM ATTITUDE TEST GIVEN TO MOTHERS OF  
EPILEPTIC ADOLESCENTS

	Positive Answer (%)
An epileptic almost always has an epileptic child -----	80
The cause of epilepsy is unknown -----	80
Epilepsy is a very mysterious disease -----	80
All epileptics have convulsions -----	70
If an epileptic eats very little, he will have fewer convulsions -----	60
Epileptic children should be protected at all times -----	50
Epileptics should be placed in a special hospital -----	60
Epileptics are incapacitated their whole life and cannot be rehabilitated -----	50
An epileptic is not good for anything -----	50
Epileptics go crazy if they do not receive treatment -----	50

#### RESUMEN

En Puerto Rico aún existe mucha ignorancia en cuanto a la condición de epilepsia. Es un problema médico en el cual todavía están encrustadas una masa de prejuicios, ignorancia e información errónea. Esta ignorancia puede verse aún en las madres de los pacientes con epilepsia, como lo demuestran los resultados de este estudio, a pesar de la oportunidad que ellas han tenido de estar cerca

de los médicos y de sus relaciones continuas con nuestra clínica de Neurología.

El propósito principal de este informe es describir el proceso de grupo empleado para ayudar a las madres de diez adolescentes con epilepsia. Este proceso era parte de una de tres fases de un programa encaminado a tratar a estos pacientes. Las madres de estos pacientes se reunieron primero semanalmente, por cinco meses y luego cada 15 días por cinco meses más, con la trabajadora social de la Clínica de Neurología, en un ambiente informal.

El propósito de estas reuniones de grupo fué aclarar las ideas erróneas que tenían las madres en relación con la epilepsia y ayudarlas a reducir sus miedos y ansiedades.

A cada madre se le dió un examen de actitud en dos ocasiones, a principio y al final de la experiencia de grupo para obtener una medida objetiva de los cambios de actitud que pudieran ocurrir.

Nueve de diez madres demostraron cambios en su actitud y sentimientos hacia la epilepsia. Una madre, a pesar de su participación en el grupo durante diez meses, aún insiste que su hija no padece de epilepsia.

Las madres de las adolescentes con epilepsia, a través del proceso de grupo y en la dinámica envuelta en el mismo pudieron cambiar muchas de sus ideas erróneas y sus miedos hacia la epilepsia.

Basándonos en esta experiencia preliminar, nosotros creemos que las adolescentes con epilepsia se beneficiaron grandemente cuando sus madres redujeron la tensión y ansiedad, obtuvieron un conocimiento claro de esta condición y su actitud fué más positiva. En nueve de diez casos, al finalizar la experiencia, el ambiente de tensión en el hogar se redujo.

El mejor tratamiento médico puede ser poco efectivo, si el paciente con epilepsia es expuesto continuamente a un ambiente de hogar psicológicamente deprimente.

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## MEDICAL DEFENSE AGAINST BIOLOGICAL WEAPONS

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The deliberate dissemination of pathogenic microorganisms to produce noneffectiveness or death in the civilian population of this country is possible if ever we should be forced into another major war.

Research on problems peculiar to defense against biological weapons and the development of concepts for providing such a defense are the responsibility of the military forces or other Federal agencies. The care of civilian casualties, however, would be the responsibility of the civilian medical profession. It is essential that physicians and ancillary medical personnel appreciate the potentials of this weapons system and consider plans for coping with the mass casualty situation which could follow its use.

The primary objective of an attack on a densely populated area probably would be the disruption of industrial, communication and transportation facilities. It would not be necessary for a high percentage of the inhabitants to become ill for an attack to be successful. If one member of a family becomes ill, others of the family would be required to care for him. The absence from work of transportation employees would create difficulties for those willing and able to report to their jobs. The psychological effects of exposure to "germ warfare" would add materially to the non-effectiveness produced. Fear and misunderstanding would be aggravated by rumor and inaccurate self-diagnosis.

Defense against a biological weapons attack is primarily a medical problem. The current military respirator and its civilian counterpart developed for civil defense use will protect an individual against microorganisms disseminated in an aerosol if the mask is being worn at the time of exposure. Facilities can be constructed and equipped so as to provide protection against such weapons but again, only those individuals inside the facility would escape exposure.

The fundamental pathology resulting from infection produced by intentionally disseminated organisms would not differ significantly from that occurring in cases of natural infection. To be sure, certain differences in the clinical picture from that with which we are familiar or which is reported in the standard texts

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may occur. "Woolsorters' disease," the respiratory form of anthrax, is quite a different problem from malignant pustule, the cutaneous form, and pneumonic plague is a much more severe disease than bubonic plague. The differences in the two forms of these diseases are determined by the route of entry of the organism, the respiratory form being more severe in each case. Certain diseases which under natural conditions are not contracted through the respiratory tract may, under artificial conditions such as we are discussing, be produced by this means. In such cases the disease may be more severe, the incubation period may be shorter and the clinical picture may differ somewhat from that seen in the naturally incurred form. The effect of the organism on the individual cell and the cellular response to the infection, however, will be unaltered.

Once clinical disease has occurred in the target population, recognition of the significance of the early cases and institution of a concerted effort to identify the etiologic agent are the most important problems with which we would have to deal. The present methods of reporting infectious disease in civilian public health systems or even in the more rigidly controlled military organization are inadequate to provide the necessary information in the time required. The Army Medical Service is now developing a program for integrating the reporting of infectious disease incidence into the Command Automatic Data Processing System being established for field army logistics and personnel management. This will provide a means for obtaining information on an hourly basis if desired. By integrating a computer capability into this system, an army or theater surgeon could be made aware within the first few hours that an unusual situation existed. This would be sufficient to set in motion additional preplanned programs to evaluate the situation more fully. Early recognition of these first cases would determine our success or failure in handling the medical problems.

If an attack with a biological agent against a military population is suspected, present Department of the Army plans call for moving selected patients to an infectious disease center where the clinical and laboratory facilities could be concentrated on obtaining an early definitive diagnosis. For an overseas area this plan might include transporting representative patients to a preselected facility in the United States where more extensive laboratory services and consultant assistance could be obtained. With reasonable precautions the danger of spreading a new infectious agent in this country would be minimal.

In order to arrive at a definitive diagnosis in time to institute an effective prophylactic program for those still in the incubation

period or to apply effective therapeutic measures for those becoming ill, all available facilities would be required. Although many of the diseases considered to have a high biological warfare potential are grippal in onset and without distinguishing characteristics, the role of the clinician in this early stage is all important. His guidance in the collection of laboratory specimens and the correlation of the clinical and laboratory data are essential. Early and accurate interpretation of x-ray findings such as the widening of the mediastinum seen in pulmonary anthrax or the rapid progression of the pneumonic process in respiratory plague may shorten by many hours the time required for institution of the proper prophylactic or therapeutic regimen. The time thus saved may be important not only in the control of the infectious process but also in preventing the panic and mass hysteria that might occur in such a situation.

The rapid identification of the etiologic agent in the event of a BW attack is one of the most difficult problems in developing an effective medical defense against this weapons system. The techniques employed are no different from those used for the diagnosis of naturally occurring disease, but the laboratory must be equipped and the personnel must be trained to apply every available method toward identifying the organism in the shortest possible time. This will require the ready availability of diagnostic antigens and antisera for the commonly encountered diseases as well as for diseases which do not occur naturally in this country. Many of these products are not available except in widely scattered research institutions. Their unavailability could delay for days the accurate identification of the disease producing agent. A wide variety of culture media and tissue culture systems must be available, adequate numbers and varieties of laboratory animals must be kept on hand, and animal holding facilities must be planned. Egg inoculation facilities must be included and equipment for handling highly infectious organisms must be provided.

A number of approaches toward a more rapid etiologic diagnosis are being investigated. Modification of culture media has resulted in a significant decrease in the time required for the identification of certain microorganisms. Microculture techniques combined with electronic scanning may provide further reduction in the time required for obtaining an accurate diagnosis.

Fluorescent antibody techniques have added to our potential for rapid identification. Jaeger<sup>1</sup> has identified Venezuelan equine encephalomyelitis virus within four hours after the collection of blood from a patient ill with the disease. A combination of tissue culture propagation and fluorescent antibody techniques was employed in this study. Rift Valley fever has been identified less

than twenty-four hours after inoculation of the tissue culture system. Smith<sup>2</sup> has isolated virus from bone marrow when it could not be isolated from peripheral blood.

Electronmicroscopy may add significantly to our capability for early diagnosis. Smith and Melnick<sup>3</sup> identified herpes virus from a vesicular lesion within three hours of collection of the specimen. The combination of electronmicroscopy, analytical ultracentrifugation, and various labelling techniques may assist materially in this area. It is not envisioned that within the near future this will become a common laboratory procedure in the small civilian hospital or the military field hospital but it certainly is feasible to incorporate such a capability into the large civilian diagnostic center or into the military base laboratory.

Metabolic changes which occur during infection are now being studied as a means for the early identification of infectious processes. There is reason to believe that the appearance of measurable amounts of unusual metabolic products or changes in the quantities of constituents normally present may occur during the incubation period. The problem is to identify these products and develop techniques for determining their presence or for recognizing subtle quantitative changes. Beisel and Sawyer in our laboratories have an extensive program in this area. Tissue biopsy or autopsy findings from individuals dying early may provide important diagnostic information.

Chromatography, electrophoresis, radioisotopes, and other elaborate laboratory procedures may contribute significantly to our capability in early diagnosis but one must not neglect the simple universally available laboratory procedures such as the Gram stain. The application of this technique may be all that is necessary to identify certain organisms, for example, *Pasteurella pestis*.

The most effective means available at this time for protection against a biological weapons attack is active immunization. Vaccines are available for a number of microorganisms that might be used against this country and additional ones are being investigated. The effectiveness of these vaccines varies considerably; 100% protection from all is not to be expected. The 17D strain of yellow fever virus for all practical purposes gives complete protection. The protection provided by triple typhoid vaccine or the living attenuated strain of *Pasteurella tularensis* is relative and a large infecting dose might well produce clinical disease. Such vaccines, however, still will have a definite place in our prophylaxis program. If they will decrease the number of persons becoming ill or the severity of the disease manifestations resulting from such illness, they will still be used. Such amelioration may mean

the difference between success or failure of a military mission or whether an important industrial or transportation complex remains operational. The mere existence of an effective immunizing procedure, however, would not necessarily deter an enemy from employing a specific agent. If the protection level in the target population is low the attack could still be successful. Yellow fever and smallpox are examples.

From a practical viewpoint, immunization for protection against an attack with biological weapons must be accomplished prior to the attack. Certain immunizations, such as those against rabies, smallpox and Q fever, may be effective if given after exposure. For each of these, the vaccine to be effective must be administered shortly after the exposure occurs. This would require immediate recognition of the attack and early identification of the specific microorganism. In planning a program of medical defense in a BW situation this approach should not be considered.

It is unlikely that in case of war the United States will have advance warning of the specific microorganism to be loosed against us. The element of surprise would be so important that the enemy would take extreme precautions to protect this information. It would be impractical to attempt to immunize the entire population of this country against all of the diseases for which we now have an immunizing product or for which one may be developed in the future. The criteria for an effective offensive weapons agent should be considered and based on the best information available; a plan for an immunoprophylaxis program should be developed. If a microorganism for which there is no effective immunizing product is included in this category a major effort to develop such a product should be made. If an effective vaccine is available, large scale production methods should be developed and stockpiling of a reasonable number of doses should be considered.

There are a number of vaccines now available for protection against diseases which are of little or no practical importance in the United States but which are of considerable significance when viewed in a possible biological warfare situation. There is little interest in such vaccines among the commercial biological manufacturers and in the medical profession interest is limited to certain research groups. It is the present plan of the Department of Defense to present certain of these vaccines to the Division of Biologics Standards of the US Public Health Service with a request for approval for military use only. The additional data required to obtain approval for general use, such as information on effectiveness and reaction rates in children, pregnant women and elderly persons would require considerably more time, money and person-

nel than is presently allotted to the military for the completion of this program.

The problems that would be encountered in a nationwide emergency immunization program would be formidable. The production of only a small number of vaccines in a limited time and in the quantity required, even if large scale production methods have been developed, would place an unprecedented load on the biologics industry. In this situation it may be necessary to forego certain sophisticated safety tests in order to provide protection for a large number in a short period of time. Production plans should include consideration of standards to be met under such emergency conditions.

The actual execution of an immunization program of this magnitude would create a number of problems. The use of the jet injection gun developed by the Army Medical Service and now commercially available would expedite such a program. The use of combined antigens would decrease the logistical load and studies in this area should be extended. The development of immunity to serologically related organisms may provide a means of obtaining protection against a large number of potential agents. Price<sup>4</sup> has demonstrated protection in monkeys against several group B arboviruses by administering live vaccines for three members of this group. Similar studies in animals have been reported for the group A arboviruses. To what extent these studies will apply in man is as yet unknown. The administration of a very small sensitizing dose of antigen to be followed, if indicated, at a later time by a full booster dose is another approach being studied.

The administration of vaccines by the aerosol route should be mentioned. The Russians have studied this subject extensively but there is no evidence that this method has been used as a practical substitute for the more conventional routes of administration. The immunization of all individuals in a large geographic area by dissemination of a vaccine from an airplane certainly has not reached the point of practical application.

The legal aspects of a compulsory immunization program in the civilian population of this country deserves study. At the present time, short of martial law, no authority exists for enforcing such a program.

If a program of immunization sufficiently broad to protect against the disease producing agents considered to be the most likely candidates for use in a biological weapons attack was instituted, would harmful effects result from the administration of the large amount of antigenic material required? Cluff<sup>5</sup> and his associates have studied this problem. Certain abnormal laboratory

findings have been observed but no evidence of clinical abnormality has been noted.

Antibiotic prophylaxis in a biological warfare situation must be considered. The use of antibiotics in anticipation of an attack is not practical. If it is known that an attack has occurred their use in the exposed population could be of considerable value. Early recognition of the attack and accurate identification of the organism is required. If the etiologic agent is susceptible to such prophylaxis the proper antibiotic and the proper dosage schedule must be determined. Scrub typhus and Q fever can both be prevented by administration of the tetracyclines but the dosage schedule for one is quite different from that for the other. Tetracycline prophylaxis for infection with *P. tularensis* is of but limited value but streptomycin will prevent the disease.

The administration of prophylactic drugs combined with active immunization might be used under certain circumstances. The use of specific immune globulin in such a situation is possible but is not considered practical at this time.

The basic principles of treatment of casualties resulting from a biological weapons attack would not differ significantly from those used in the treatment of patients with naturally occurring disease. In the event of a successful attack a mass casualty situation would exist but the requirements for medical facilities would be considerably less than those resulting from an attack with nuclear weapons. Extensive resuscitation and surgical facilities would not be required. Most individuals becoming ill would be able to get to their homes where they could be cared for and treated. Once a diagnosis was established extensive laboratory procedures would not be required and the care available in the home would be adequate for the majority.

There are additional important differences between the medical planning required for a biological weapons attack and that required for a nuclear attack. In an attack with a biological weapon, unless preceded or accompanied by other means of warfare, physical facilities, transportation, communications, and medical supplies would be intact. Medical personnel, however, would be affected in the same ratio as the total population. In a nuclear attack the majority of casualties will occur in a matter of seconds or minutes. Casualties occurring after the intentional dissemination of pathogenic organisms will occur over a period of days or even weeks. If the first cases are recognized and appropriate preplanned actions are instituted, the difficulties in coping with the problem will be reduced significantly.

The response to the antibiotics would be similar to that for the same disease incurred by natural means if an artificially pro-

duced antibiotic resistant strain is not employed. Radio, television and newspapers could be used for the dissemination of information regarding medical care. If an agent were employed which produced a disease for which there was no specific therapy and which resulted in a high percentage of deaths, the problem of home care would be considerably more difficult, but with our present knowledge there is no practical alternative. Even with so-called non-lethal agents some deaths will result. These are to be expected in infants, elderly people and those already suffering from serious disease.

There are many problems associated with developing an adequate medical defense against a biological weapons attack. Some of these will not be answered until such an attack is actually encountered in a war situation. I would like at this point, to make some specific suggestions toward developing a civilian defensive capability against this weapons system.

1. The feasibility of this weapons system and the potential threat to this country in case of war should be kept under constant review.

2. Training in infectious disease in medical schools, local, county, and state medical societies, and in our national medical organizations should be increased.

3. Ancillary medical personnel should be trained in the defensive aspects of biological warfare.

4. A concerted effort should be made to increase the level of immunity in the civilian population against those diseases for which protection under normal conditions is considered desirable, for example, smallpox, tetanus, diphtheria, typhoid fever and others.

5. Diagnostic centers with the capability of studying a wide range of infectious diseases should be established and, if necessary, subsidized by Federal agencies.

6. Plans should be made for the use of radio, television, and newspapers to alleviate fear and prevent panic as well as to disseminate instructions for medical care.

7. Up-to-date inventories of antibiotics available in a geographical area should be maintained. Requirements and plans for movement of drugs from one area to another should be established.

8. The legal aspects of compulsory immunization should be studied and perhaps new legislation sought.

These are practical suggestions that can be instituted without large outlays of funds or personnel, and which can be accomplished without disruption of the medical economy. There are others but if those listed are considered seriously, a significant step toward improving our medical defensive capability against biological weapons will have been made.

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**CONSULTA MEDICA.**

Consulta médica se define por el diccionario de La Real Academia Española, edición 1956, como una reunión de médicos para hallarle solución a algún problema.

Hasta hace algunos años la consulta médica se llevaba a cabo de una manera muy distinta a lo que se estila hoy en día. Entonces la consulta médica se ejercía en la casa del enfermo. Esta era solicitada por el propio enfermo o por sus más allegados familiares o por el galeno de cabecera quien se encargaba de llamar a los compañeros que él creía necesario o a los médicos de los familiares o de amigos íntimos del enfermo. Se acordaba la hora y día de la consulta la cual se celebraba primero en la sala de la casa. En la consulta, muchas veces, se empezaba a hablar de todo menos del enfermo pero, finalmente, el médico de cabecera explicaba detalladamente los pormenores de la enfermedad y el tratamiento dado hasta el momento. El número de médicos llamados podía variar de uno a varios, generalmente varios, y al terminar el médico de cabecera de exponer los detalles de la enfermedad, cada uno de los médicos pasaba a la habitación donde estaba el enfermo y generalmente uno procedía a examinar al paciente y los otros esperaban su turno. Al terminar esta fase de la consulta todos los médicos presentes se reunían en la sala de nuevo para seguir la discusión sobre los hallazgos de los distintos exámenes y se procedía entonces a llegar a un acuerdo en cuanto a qué se debería hacer de ahí en adelante. Finalmente se invitaba a los familiares más allegados a oír la opinión de los consultores o se visitaba de nuevo al enfermo para explicarle los resultados de la reunión.

Este tipo de consulta ha ido desapareciendo. En nuestra época el hospital ha adquirido tanta importancia que la mayoría de los enfermos que necesitan de ciertos estudios son recluidos y cuando es necesaria una consulta, ésta se lleva a cabo en el hospital pero el procedimiento ha variado mucho. Es importante el evitar aceptar ver un enfermo en consulta a menos que el médico de cabecera le indique a uno su deseo de que uno vea al enfermo como consultor. Muchas veces familiares o hasta amigos llaman a un médico para pedirle que vea a un enfermo que está bajo tratamiento con otro compañero y me parece un deber el rehusar cortesmente ese tipo de petición.

En ocasiones el médico de cabecera le indica a los familiares o amigos su supuesta conformidad a que la consulta se lleve a ca-

bo. No creo correcto que el médico de cabecera olvide que es su deber y además el método ético, el que él mismo sea quien llame al compañero consultor y aproveche no solamente para invitarle a la consulta, sino para explicarle el porqué de la misma y los detalles de la enfermedad que ha podido obtener durante los días que ha visto al enfermo.

Con gran frecuencia, hoy en día, recibe uno una llamada de una enfermera para informarle que tal médico desea una consulta con tal enfermo. A pesar de que, debido a numerosas razones, ésto sea lícito, creo que lo correcto debe ser siempre que el médico de cabecera, por lo menos, hable con el médico consultor aunque sea por teléfono y así se puede transmitir información pertinente que pueda ser de utilidad y en beneficio del enfermo. Con frecuencia, cuando el médico de cabecera y el consultor no han podido hablar antes de la consulta, el médico de cabecera o uno de los internos o residentes ha escrito unas cuantas palabras, con frecuencia muy pocas, a veces ilegibles, en la hoja de consulta. Lo ideal sigue siendo igual que lo era en antaño, que la consulta sea una cosa más enjundiosa de lo que usualmente resulta. Desgraciadamente nuestro progreso ha reducido la consulta médica a la expresión unilateral de opiniones. Tratemos de evitar que esto suceda.

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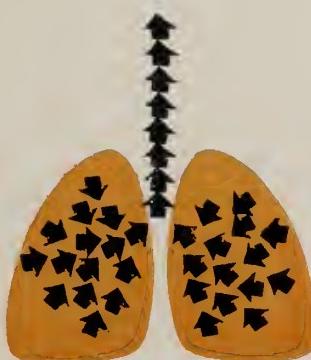
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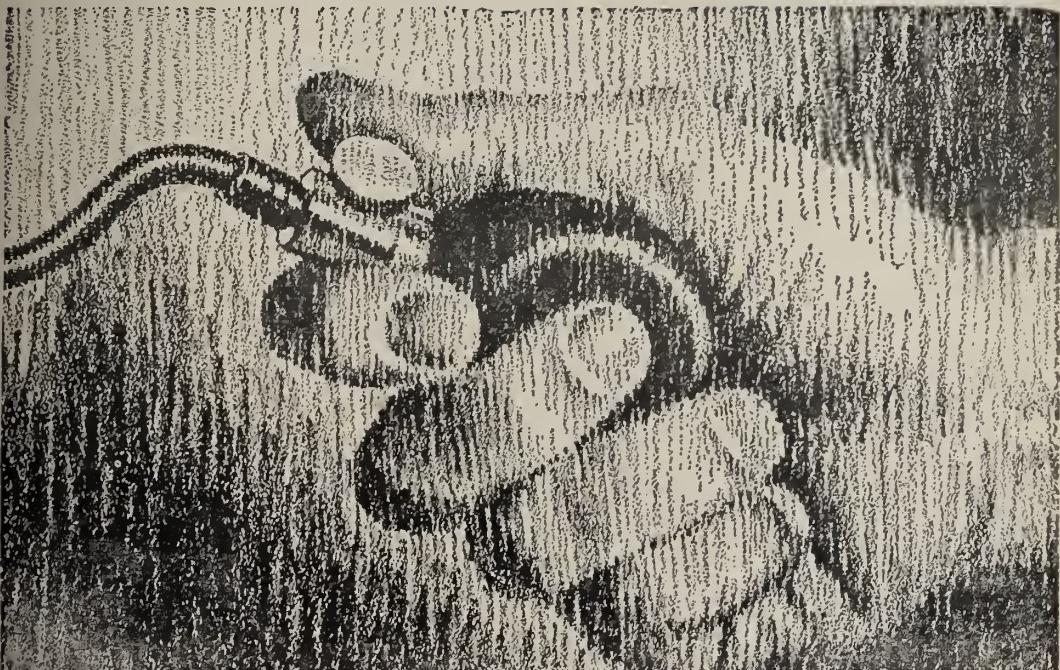
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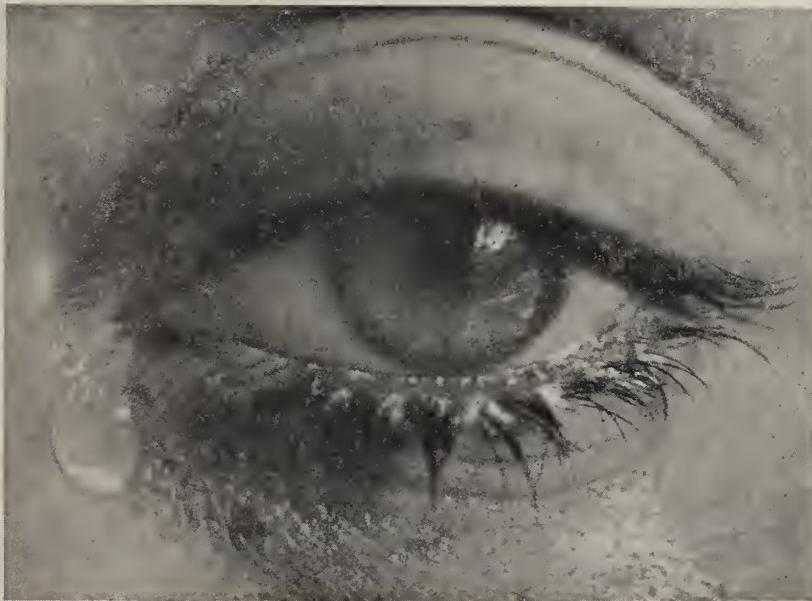
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i) Las fotografías y microfotografías se someterán como copias en papel de lustre sin montar. Los dibujos y gráficas deben prepararse a tinta negra y en papel blanco. Todas las ilustraciones deben estar numeradas (números árabigos) e indicar la parte superior de las mismas. Debe escribirse una leyenda para cada ilustración e indicarse en el texto donde debe ir colocada. Un máximo de 6 ilustraciones, por artículo, serán permitidas sin costo para el autor.

j) Las referencias deben ser numeradas sucesivamente de acuerdo con su aparición en el texto. Los siguientes ejemplos pueden servir de modelo:

6. Koppisch, E. Pathology of arteriosclerosis. Bol. Asoc. Med. P. Rico 46: 505, 1954. (artículo de revista)

4. Wintrobe, M. M. Clinical Hematology, 3rd Ed. Lea and Febiger, Philadelphia, 1952, p. 67. (libro)

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Se podrán ordenar sobretiros del artículo cuando se reciba notificación de su aceptación.

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The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the understanding that it is to be published solely in this journal.

In order to facilitate review of the article by the Editorial Board and the preparation of the manuscripts for the printer the authors are requested to follow the following instructions:

a) The entire manuscript, including figure legends and references, should be typewritten double-spaced in duplicate with ample margins.

b) A separate title page should include the following: title (not to exceed 80 characters and spaces), author(s) names and academic degrees, institution, and authors' mailing address.

c) Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: (1) introduction, (2) material and methods, (3) results, (4) discussion, (5) summary in English and Spanish, (6) references.

d) Case reports will include (1) introduction, (2) description of the case, (3) discussion, (4) summary in English and Spanish and (5) references.

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g) Generic names of drugs should be used. Trade names may also be given in parenthesis if desired.

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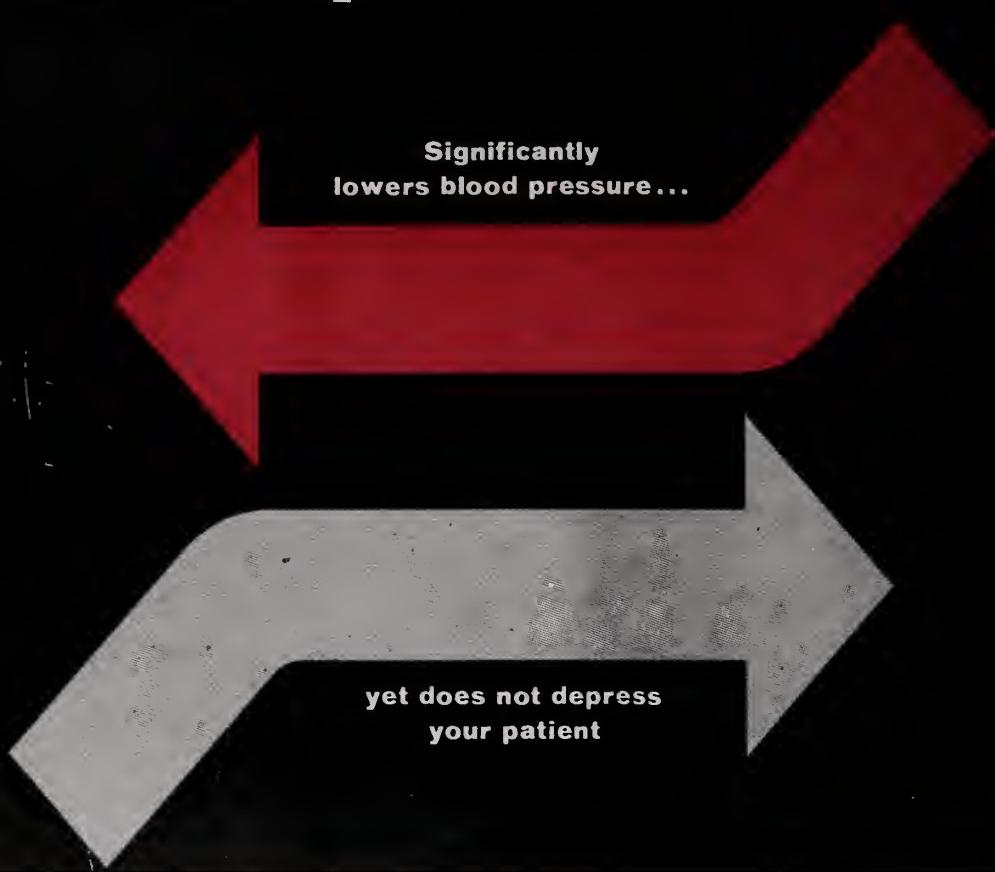
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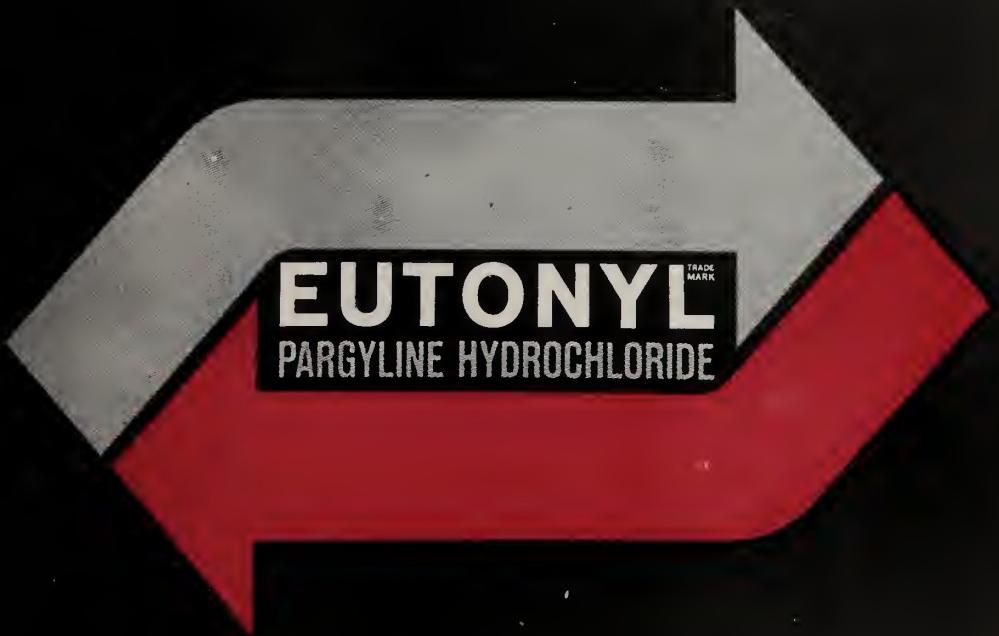
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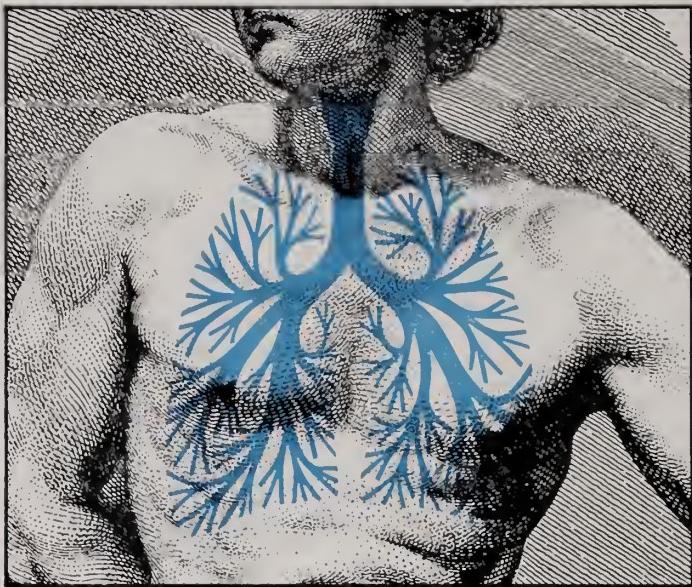
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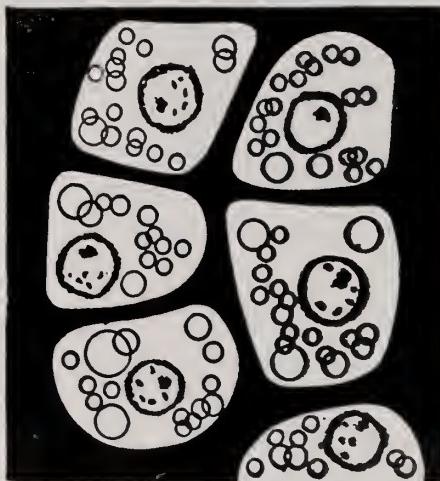
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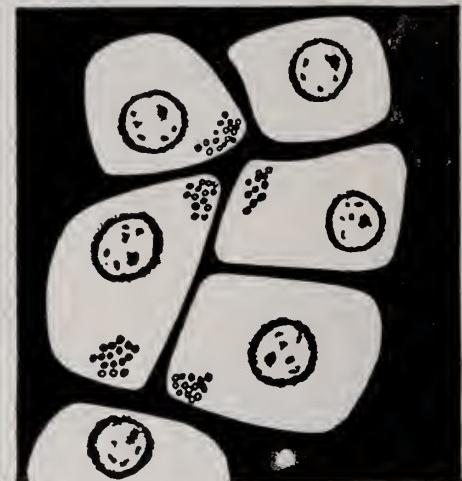
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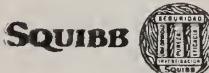


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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



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# BOLETIN

DE LA ASOCIACION MEDICA DE PUERTO RICO

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VOL. 56

MARZO, 1964

NO. 3

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## FOREIGN BODY IN THE ESOPHAGUS SIMULATING MYOCARDIAL INFARCTION\*

JOSE M. TORRES-GOMEZ, M.D.

Santurce, P. R.

In these days when the least learned of the laity feel that they are proficient enough to discuss different manifestations of coronary artery disease, the adequate interpretation of anterior chest pain by the physician, is most important. It is getting to be so easy to fall prey to the making of the diagnosis of angina pectoris in the absence of essential evidence, and so difficult to change a patient's mind when he has already made his own diagnosis, that the physician participates too frequently in the erroneous acceptance of both situations. Perhaps, it may be worse to label a patient "cardiac" when he is not, than to miss the diagnosis of coronary artery disease in a given individual at a given instance. It is with these thoughts in mind that the following case is presented.

### Case Report:

A man of 65 years of age was admitted to Doctor's Hospital in the night of January 27, 1956 complaining of very severe retrosternal pain. He was described as being in acute distress but there was no element of shock. There was no dyspnea. Blood pressure, 200/100; pulse, 96/min.; respirations, 28/min. Following his supper, after he had swallowed a pill which he had been taking for weeks, he suddenly developed anterior chest pain. It became so severe and persistent that he was brought to the hospital not long after the pain had started. He was a known hypertensive who had suffered one previous well documented episode of myocardial infarction. His two brothers had died of myocardial infarction. The possibility of another acute myocardial infarction could hardly be rejected at this moment, and 100 mgm. of De-

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\* Presented at the Annual Meeting of the P. R. Medical Association,  
November 1963.

merol were immediately given on admission to alleviate his pain. There were no audible murmurs, no arrhythmias, and no signs of congestive heart failure. Oxygen was started via nasal catheter and the patient was placed on absolute bed rest. In the morning of the 28th, his pain required additional doses of Demerol. However, closer observation later in the afternoon revealed that his pain was brought forth mainly on talking or swallowing, and that he felt better while in the sitting position. Though everything seemed to point toward an infarct initially, some doubt as to the validity of this diagnosis began to appear in our minds. The electrocardiogram (EKG) taken on the evening of the 28th disclosed T wave inversion in L<sub>1</sub>, VL, V<sub>5</sub>, and V<sub>6</sub>, but since by now the pain seemed to be closely associated with swallowing, we had to make certain that these EKG changes were of recent origin (Fig. 1). Moreover, the erythrocyte sedimentation rate was 4mm/hr., the patient had been afebrile, and leucocytosis was not evident (7,250-60% seg.). Since an EKG had been obtained from this patient about 4 months prior to this admission, it was requested for comparison with the present ones. The diagnosis of myocardial infarction was less tenable when both EKGs were found to be practically identical (Fig. 1).

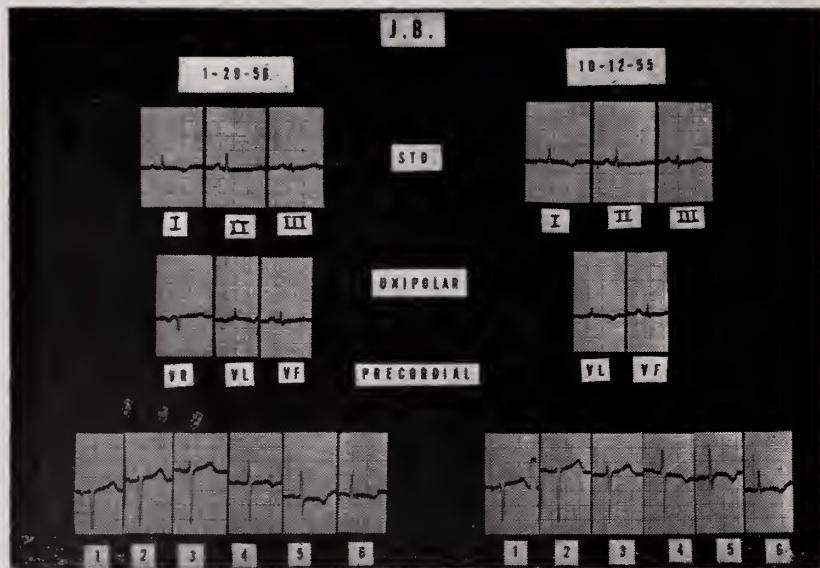


Fig. 1: Electrocardiograms showing identical T-wave abnormalities on October 12, 1955 and January 29, 1956.

Since the pain, though of less intensity, persisted on swallowing, the patient was taken on a wheelchair to the Radiology Department, and a barium swallow was performed with great care

on January 30, 1956, his second hospital day. The cardiac shadow had a normal configuration. The esophageal studies revealed a para-esophageal hernia (Fig. 2, 3, 4). The patient was then treated with anti-acids and anti-cholinergics but the pain remained unaltered. It was the feeling of those who saw the patient, that the esophageal hernia alone was not enough to explain his pain. A surgeon and ENT specialist were consulted, and the decision to perform an esophagoscopy was made. It was carried out on February 1, 1956 (4th hospital day). To everyone's surprise, a thin round piece of bone of about 2cm. in diameter was found in the lowermost part of the esophagus and removed (Fig. 5). As soon as this procedure was completed, the patient became asymptomatic. He was discharged on the following day. On questioning the patient again, he revealed that the night he developed the pain he had soup as part of this supper. In all probability, he swallowed the piece of bone while drinking his soup.

The films of the barium swallow were examined in retrospect but in none of them could the bone be identified. This was a bit puzzling since the bone was not demineralized. Direct films of the bone confirmed this, as an adequate shadow was cast in both A-P and lateral views. With the valuable assistance of Dr. Laszlo Ehrlich, Chief of the Radiology Service at the Veterans Administration Hospital, further experimenting led us to place the bone over the skin of another person so that when the picture was taken, the shadow of the bone would appear more or less at the esophageal site where it was found. After several tries, it was discovered that only when the bone was caught in its straight lateral view, could a noticeable radio-opaque shadow be produced (Fig. 6). Apparently, none of the films that were taken on the patient caught the bone in this precise angle. Otherwise, its presence would have been detected.

#### DISCUSSION

This case serves to emphasize several points that we should be constantly aware of while practicing cardiology. First, do not label a patient "cardiac" until the essential evidence is there to substantiate the diagnosis. In this instance, even though we were dealing with a known cardiac who had had a previous coronary occlusion and who now showed an abnormal EKG, the pain had a different origin. Second, clinical observation and an adequate history are still most important in arriving at a correct diagnosis. Even though this man's pain had the location and other characteristics frequently seen during an episode of acute coronary occlusion, the observation that it occurred mainly on swallowing gave the clue to the real cause of his distress. Third, not every retros-

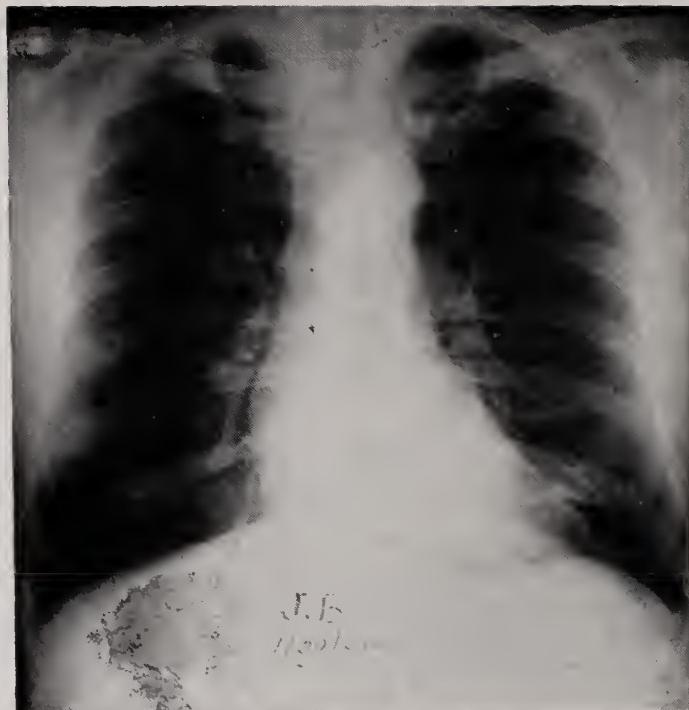


Fig. 2: Roentgenograms of the chest (PA) on January 30, 1956 showing no abnormality.

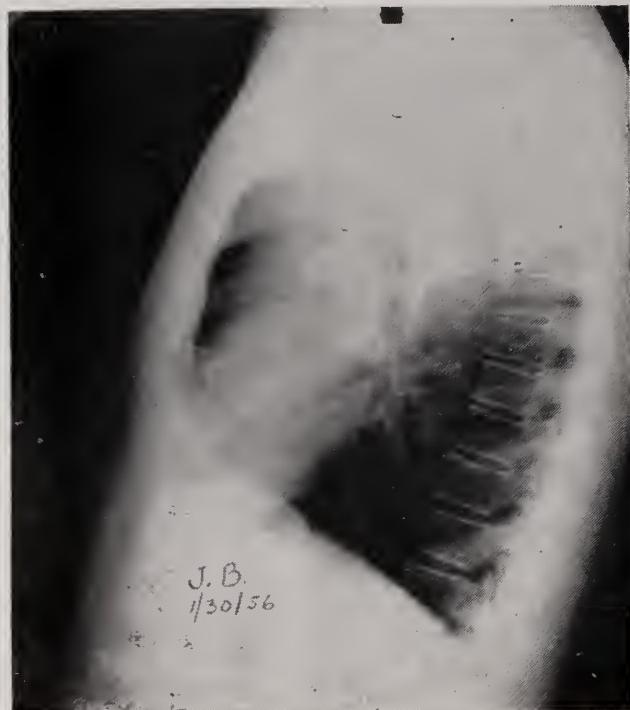


Fig. 3: Lateral view, also normal.



Fig. 4. Barium study demonstrating para-esophageal hernia but no other abnormality.



Fig. 5: Photograph of bone removed showing adhering barium from study performed the day before.



Fig. 6: Composite roentgenograms showing (left) bone undetected when placed flat on the surface of the skin and (right) being visible when placed paravell to the X-ray beam.

ternal or mid-anterior chest pain per se means coronary insufficiency or angina pectoris. There are certain basic criteria that have to be satisfied before we accept these diagnosis. And fourth, do not let negative radiographic examinations discourage you when you feel clinically sure that your suspicion is sound. In this case we have seen a bone proven through subsequent radiographic filming to be radio-opaque, yet its presence could not be detected on the patient's X-ray studies even in retrospect examination.

#### SUMMARY

An interesting case is discussed wherein a patient who had definite evidence of coronary artery disease presented himself with acute retrosternal pain, which contrary to initial expectations, turned out to be caused by a soup-bone that was swallowed and had lodged itself in the area of a para-esophageal hernia. Adequate clinical observation was mainly responsible for the making of the correct diagnosis and the cure of the patient.

#### RESUMEN

Se presenta un caso interesante en el cual un conocido paciente cardiaco (arterioesclerosis) desarrolla un dolor agudo retroesternal simulando un infarto del miocardio. Estudios subsiguientes revelaron que el dolor se debía a un hueso que el paciente

se había tragado y había quedado encasillado en una hernia paroesofágica. Se hizo finalmente el diagnóstico correcto siguiendo más bien la observación clínica que lo que indicaba el estudio radiográfico.

## HEPATOPATIAS DE LA INFANCIA QUE PRODUCEN CIRROSIS\*

MARIO E. RAVELO MARCHENA, M.D.\*\*

Desde hace algunos años hemos venido observando la frecuencia de cirrosis hepática en los niños admitidos al Hospital Infantil. Estos niños pertenecen a las esferas más bajas de nuestro país, viven hacinados y están en su inmensa mayoría desnutridos. Su dieta es rica en hidrocarbonados, pero muy pobre o nula en prótidos, de ahí que los casos de desnutrición grave (Kwashiorkor) abunden en nuestras camas de hospital.

Hemos pensado en la relación posible entre la etiología y causas coadyuvantes de nuestras cirrosis, con las cirrosis infantiles de otros países donde esta enfermedad es frecuente y su status socio-económico similar al nuestro. Entre las más importantes encontramos la observada en África en la tribu Bantu cuyos habitantes tienen una dieta similar a los nuestros. La que se observa en los negros de Jamaica, descrita por Bras, Jelliffe y otros como Enfermedad Veno-oclusiva que es producida, según ellos, por la ingestión de tisanas de un tóxico hepático (Senecio).<sup>1,2</sup> La de los niños en la India que ha sido considerada por algunos como una forma atípica de Hepatitis viral.<sup>3</sup>

Es el propósito de este trabajo hacer un estudio de nuestras cirrosis, comparándolas con las que se observan en otras áreas geográficas, establecer su incidencia en nuestro medio, clasificarlas y determinar en lo posible sus causas.

### MATERIAL Y METODOS

Se estudiaron las secciones de Hígado correspondientes a los años 1962 y 63, que incluían 75 autópsias y 82 biopsias, entre ellas 5 biopsias en cuña y el resto por punción. Se descartaron todos aquellos casos que no se consideraron pertinentes al problema que nos ocupa y sólo se conservaron aquellos casos generalmente aceptados como capaces de producir cirrosis o por lo menos contribuir a su formación. Se incluyeron por supuesto todas las cirrosis diagnosticadas en nuestras series. Se seleccionaron sólo 88 casos distribuidos como se indica en el CUADRO I.

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## CUADRO I

Hepatitis viral	22	casos
Degeneración grasa del hígado*	37	"
Anemia falciforme o falcemia	7	"
Cirrosis biliar	7	"
Cirrosis portal	2	"
Cirrosis post-hepatitis	8	"
Cirrosis post-necrótica	3	"
Cáncer trabecular del hígado	1	"
Cirrosis no clasificada	1	"

Las secciones fueron fijadas en formol al 10%, incluidas a la parafina y cortadas a 4, 5, y 6 micras. Coloreadas con hematoxilina-floxina como coloración de rutina. Se usaron los Tricrómicos de Masson al azul de anilina y al azafrán, para demostrar el tejido conectivo cuando fue necesario. Sólo muy ocasionalmente se usó otra coloración.

## OBSERVACIONES

Las secciones fueron revisadas tratando de clasificarlas dentro de los diagnósticos admitidos y usados por casi todos los autores y dentro de la mayor precisión posible.

**Hepatitis Viral:** Se consiguieron 22 casos de hepatitis infecciosa, que se distribuyeron de la siguiente manera: Hepatitis aguda 9 casos, hepatitis residual 2, hepatitis crónica recidivante 10, hepatitis de células gigantes 1.

**Hepatitis aguda.** Para el diagnóstico de hepatitis aguda se utilizó el siguiente criterio.<sup>4</sup>: 1—Distorsión de la arquitectura lobulillar, debido a la hinchazón de las células hepáticas. 2—Células hepáticas muy aumentadas de tamaño con citoplasmas ópticamente vacíos o finamente grumosos y transparentes. 3—Infiltración portal por histiocitos, plasmocitos, neutrófilos y algunos eosinófilos. 4—Infiltración de estas mismas células dentro de los lobulillos, invadiéndolos desde la periferia. 5—Necrosis hialina de células hepáticas aisladas, los llamados cuerpos de Councilman. 6—Evidencia de regeneración, como mitosis, células binucleadas y proliferación de conductillos biliares. 7—Estasis biliar. Una o dos de estas últimas condiciones faltaron ocasionalmente. Los síntomas más frecuentes eran trastornos gastro-intestinales, fiebre, hepatomegalia, bilirrubinemia, urobilinuria, Hanger positivo de 3 a 4 cruces, ictericia sólo en 5 de los casos (4 anictéricos). Las edades iban desde 1 año y 3 meses hasta los 13 años.

\* Entre los casos de Degeneración grasa, sólo se incluyeron aquellos con esteatosis moderada o severa del hígado, inclusive aquellos con fibrosis portal.

Se incluyó dentro de este grupo un caso que histológicamente correspondía a la llamada Hepatitis de células gigantes<sup>5</sup> debido a que además de simular morfológicamente una hepatitis viral, los síntomas correspondían a los de esta enfermedad (3 años, masc., ictericia, fiebre, hepatomegalia, etc.) Sin embargo, a pesar de que la hepatitis de células gigantes ha sido considerada por algunos, como una forma atípica de hepatitis viral<sup>6,7</sup> nosotros hemos visto estos cambios en condiciones muy variadas, especialmente en atresia de vías biliares<sup>8</sup> y la consideramos como una reacción inespecífica del hígado a diversas formas de injuria.

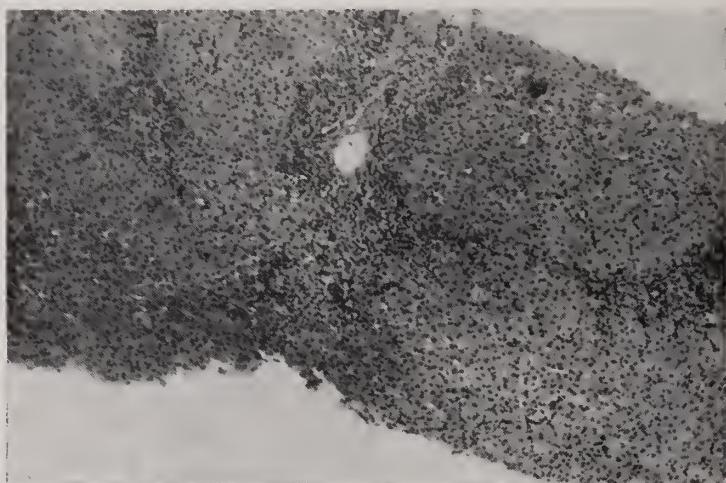


Figura 1. Hepatitis viral aguda. Punción biopsia.

**Hepatitis residual.** (2 casos) Hemos dado en llamar estos casos hepatitis residual, porque en ellos se observan todos los cambios morfológicos descritos anteriormente, pero en forma muy atenuada. La estasis biliar es nula, los corpúsculos hialinos están ausentes o son muy escasos. También el infiltrado inflamatorio es discreto. En ninguno de los casos estaban presentes los síntomas clásicos de la enfermedad y no había ictericia.

Nosotros interpretamos estos casos como un estado de convalecencia hacia la curación definitiva.

**Hepatitis crónica recidivante** (11 casos).<sup>9,10,11</sup> Se clasificaron dentro de este grupo aquellos casos en los cuales la duración de los síntomas había sido excesivamente larga (5 meses a 1 año). Se había sospechado el diagnóstico por la historia y las pruebas hepáticas. Los síntomas aparecían y luego mejoraban por períodos variables; hacían febrículas, ictericia y trastornos digestivos de vez en cuando, algunos mostraban edema de las extremidades inferiores y comenzaba a observarse circulación colateral en el abdomen y ascitis. Sólo 6 de los 11 casos estaban ictericos en el mo-

mento de la punción. Las secciones mostraron grandes zonas de destrucción del parenquima hepático y su reemplazo por fibrosis. En estas áreas se observó abundante proliferación de los conductillos biliares y un denso infiltrado de células redondas, entre las que se encontraban ocasionalmente algunos eosinófilos. Las células hepáticas estaban hinchadas con su citoplasma finamente grumoso o translúcido. Se observó intento de regeneración del parenquima con gran abundancia de células binucleadas y mitosis frecuentes. No se encontró estasis biliar y sólo muy rara vez cuerpos hialinos.

No encontramos en estos casos suficiente evidencia morfológica para incluirlos dentro de las cirrosis. Creemos más bien que se trata de formas severas de hepatitis en las cuales ha habido extensa destrucción del parénquima hepático, que no han curado dentro del plazo corriente para formas más benignas y cuyo curso tórpido los lleva con casi toda seguridad al desarrollo de una cirrosis post-hepatitis.

No encontramos en nuestro material ningún ejemplo de hepatitis fatal.<sup>10,11</sup>

**Degeneración grasa.** Se reunieron 37 casos de degeneración grasa entre formas moderadas y severas, casi todos los cuales correspondían a formas clínicas de desnutrición (nanismo, desnutrición grave, tipos marasmático y edematoso).<sup>12</sup> Se incluyeron también 3 casos de Mucovicidosis.

Las secciones mostraron vacuolización y deposición de lípidos dentro de las células hepáticas principalmente alrededor de los espacios porta en las etapas iniciales, aunque a menudo no se observó una localización específica sino más bien difusa. En los 3



Figura 2. Hepatitis viral crónica. Punción biopsia. Se observa abundante tejido cicatricial.

casos de enfermedad fibroquística del pancreas, la esteatosis sí se localizaba definitivamente alrededor de los espacios porta y se encontró fibrosis de los mismos.

En los casos diagnosticados como degeneración grasa severa, los cuales con raras excepciones correspondían a formas graves de desnutrición, se vió degeneración grasa de casi todas las células hepáticas incluidas en las secciones y fusión de varias de ellas en cada lobulillo, formando pequeños quistes bordeados por varios núcleos.<sup>13</sup> Ocasionalmente se encontraron necrosis focales de algunas células o grupos de células. Los espacios porta estaban infiltrados por linfocitos, plasmocitos, e histiocitos.

Consideramos estos cambios como característicos de las formas graves de desnutrición.

En un último grupo (4 casos) se veía proliferación de fibroblastos y deposición de fibras colágenas tratando de unir áreas portales vecinas. Para algunos<sup>14</sup> esto se interpreta ya, como la etapa más temprana de una cirrosis portal. No dudamos que esto sea así, pero debido a la ausencia de desorganización obvia de la estructura lobulillar normal, preferimos abstenernos de llamar cirrosis a estos casos.



Figura 3. Cirrosis post-hepatitis en la evolución de una hepatitis viral. Punción biopsia.

**Anemia falciforme y falcemia.** Esta forma de anemia es muy común en nuestro medio y como a menudo produce hepatomegalia, hemos tenido oportunidad de estudiar algunas punciones (4 casos).

Lo que más llama la atención al estudio microscópico es la congestión de moderada a severa de los sinusoides hepáticos, que a veces parecen formar pequeños lagos llenos de hematíes deformados "bananitos". Aquí y allá encontramos verdaderos tapones de

hematíes característicos y alrededor de ellos áres de necrosis isquémica de grupos, a veces bastante prominentes de células hepáticas. Las células de Kupffer están cargadas de hemosiderina. En focos aislados se ha observado cierto grado de estasis biliar. Una de las secciones mostró fibrosis portal.

Se ha descrito la anemia falciforme como causa de cirrosis,<sup>15,16</sup> pero ninguno de nuestros casos reunía estas condiciones.

En los 3 casos en que estuvo presente la deformación (falcemia) pero que no tuvieron anemia falsiforme, se observó al estudio de las secciones la misma congestión de los sinusoides, pero no había tapones, ni se encontraron zonas de necrosis o fibrosis portal.

**Cirrosis biliar.** Se diagnosticaron como cirrosis biliar aquellos casos en los cuales se comprobó quirúrgicamente o a la autopsia; atresia congénita de las vías biliares extra-hepáticas (4 casos) o intrahepáticas (2 casos) y en los cuales había fibrosis portal marcada.

En los casos de atrasia de las vías biliares extra-hepáticas, las secciones mostraban fibrosis extensa de los espacios porta y proliferación abundante de los conductillos biliares en estas mismas áreas.<sup>17,18</sup> En 3 de los casos el parenquima parecía normal excepto por grados variables de estasis biliar. El otro caso presentaba el aspecto histológico de una hepatitis a células gigantes, con células multinucleadas rodeando lagunas de bilis.<sup>8</sup>

En los casos de atresia intra-hepática de vías biliares, los cambios más llamativos estaban en los espacios porta, pero de manera diferente a los anteriores. Los conductillos biliares eran muy escasos o no se veían por ninguna parte. Tenían el aspecto de sólidos cordones de células cúbicas, carecían de luz, parecían salir de los lobulillos (perfectamente bien formados) pero no alcanzaban a penetrar de lleno en las áreas portales. Se encontró fibrosis de estas áreas pero en mucho menor grado que en las atresias biliares extrahepáticas.

**Cirrosis.** Para la clasificación de las cirrosis<sup>19,20</sup> (excluyendo cirrosis biliar) hemos usado el criterio de Gall<sup>21</sup> modificado por nosotros. Ver CUADRO II.

**Cirrosis portal:** Se estudiaron 2 casos diagnosticados por nosotros como cirrosis de tipo portal. Las secciones mostraban extensa fibrosis, que rodeaba pequeños pseudolóbulos generalmente esféricos, en los cuales había abundante degeneración grasa de las células hepáticas. Las trabéculas conectivas eran gruesas y contenían gran cantidad de conductillos biliares en franca regeneración. Se encontró infiltración difusa del tejido fibroso por linfocitos, plasmocitos y algunos granulocitos neutrófilos. La estructura

## CUADRO II

DIAGNOSTICO DIFERENCIAL MICROSCOPICO DE LAS CIRROSIS		
CIRROSIS PORTAL (o Nutricional)	CIRROSIS POST- HEPATITIS	CIRROSIS POST- NECROTICA
Pseudolóbulos de aproximadamente igual tamaño, pequeños y de forma redondeada.	Lóbulo único o grupos de lóbulos rodeados por delgadas trabéculas de tejido conectivo.	Pseudolóbulos redondeados de tamaño muy variable entre ellos.
Trama gruesa de fibrosis que rodea los pseudolobulillos.	Áreas de fibrosis en forma estrellada, de la cual parten delgadas trabéculas conectivas.	Zonas cicatriciales anchas que agrupan dos o más espacios portales.
Degeneración grasa severa.	Infiltración del tejido conectivo y de la periferia de los lobulillos por tejido linfoides.	Infiltración difusa de las áreas cicatriciales por linfocitos, plasmocitos, monocitos y neutrófilos. Proliferación de los conductillos biliares.
	Los lobulillos hepáticos conservan su estructura normal, con sus venas centrolobulares. La célula hepática es de apariencia normal.	Los pseudolóbulos muestran nódulos de hiperplasia. Se observan áreas de necrosis isquémica, por compresión de los vasos.
	No hay degeneración grasa.	No hay degeneración o ésta es mínima, excepto en desnutridos (Kwashiorkor).

normal estaba radicalmente perdida y no se observó evidencia de regeneración en las secciones examinadas.

**Cirrosis post-hepatitis.** Los 8 casos clasificados dentro de este grupo mostraban fases sucesivas de evolución desde hepatitis crónica con cirrosis inicial hasta esclerosis cicatricial del hígado. En la fase más temprana fue a veces muy difícil hacer una delimitación categórica entre hepatitis crónica y cirrosis incipiente. En la etapa más temprana se observaron los cambios más devastadores. Las secciones mostraban aún los cambios correspondientes a la hepatitis viral. Las células hepáticas estaban hinchadas dos o tres veces su tamaño normal, su citoplasma era pálido o finamente granuloso. Todavía se encontraban, aunque ocasionalmente corpúsculos hialinos. Había un denso infiltrado de células redondas y algunos eosinófilos en el tejido conectivo y dentro de los lobulillos. También se observó estasis biliar en algunas áreas. Las zonas de necrosis eran extensas; en ellas se encontraban numerosos vestigios celulares, tales como fragmentos nucleares, núcleos en picnosis, etc. El tejido reticular estaba intacto en el área más cercana al parénquima menos dañado. El resto había sido reem-



Figura 4. Cirrosis post-hepatitis más avanzada que la anterior. Material de autopsia.

plazado por fibrosis. Dentro de esta fibrosis se veían conductos biliares regenerándose en una forma bastante característica. Se hallaron grupos de conductos vecinos que emitían proyecciones papilares dentro de su luz o parecían enroscados sobre sí mismos, produciendo la imagen de una hiperplasia adenomatosa. En algunas áreas, se observaba también hiperplasia regenerativa de las células hepáticas formando grupos más compactos, de citoplasma lleno, con uno o dos núcleos aumentados de tamaño e hipercromáticos, islotes estos que resaltaban sobre el resto de la sección.

En la fase más tardía la evidencia de hepatitis generalmente faltaba. La estructura lobulillar normal estaba bastante distorsionada. Las secciones mostraban grandes pseudolóbulos de forma irregular y sinuosa formados por la fusión de varios lobulillos. Dentro de cada uno de estos pseudolóbulos se podían encontrar de dos a cinco venas centrolobulillares. Se veían cicatrices de forma estrellada, de donde partían delgadas bandas de tejido conectivo rodeando los islotes de parenquima hepático. A lo largo de estas trabéculas conectivas, de manera dispersa, se encontraron colecciones de linfocitos, verdaderos nódulos linfáticos. De los que fueron espacios porta sólo quedaban grupos de conductillos biliares en la forma adenomatosa descrita antes. El parenquima hepático parecía normal, los núcleos eran algo hipercromáticos, tal vez estaban aumentados de tamaño, pero nada más. No se observó degeneración grasa por ninguna parte o ésta era mínima.

**Cirrosis post-necrótica.** Sólo 3 casos, 2 punciones y 1 autopsia correspondían a este tipo de cirrosis.

Las secciones mostraban destrucción total de la estructura hepática normal. Los pseudolóbulos eran de forma redondeada y

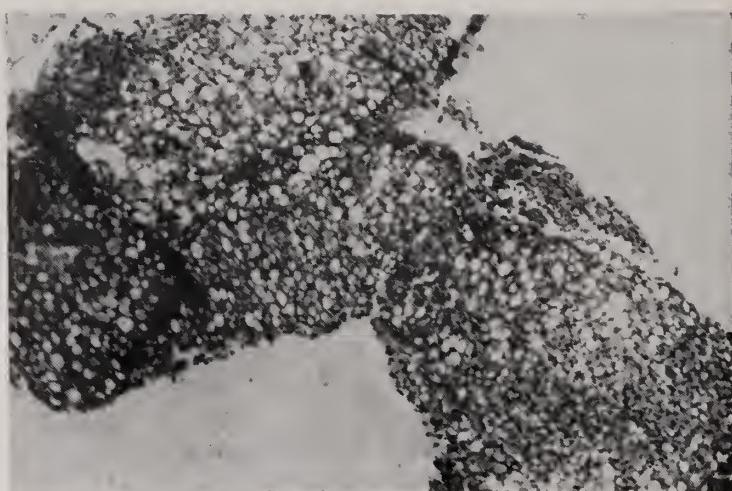


Figura 5. Degeneración grasa del hígado, severa. Kwashiorkor. Punción biopsia.

de tamaño variable, algunos de más de 1 cm. de diámetro. Se observaron anchas zonas cicatriciales que agrupaban varios espacios porta, en las cuales se veían venas muy dilatadas, engurgitadas de sangre. Fué casi imposible identificar las venas centro-lobulillares. Las áreas cicatriciales estaban infiltradas por células redondas y algunos neutrófilos, había proliferación y multiplicación de conductillos biliares. En algunas áreas la regeneración de las células hepáticas era muy prominente y simulaban verdaderos adenomas trabeculares.<sup>22</sup> En otras, se observó necrosis isquémica de algunos pseudolóbulos, posiblemente debida a la compresión de los vasos por el aumento de tamaño de los nódulos en regeneración.



Figura 6. Cirrosis post-necrótica. Extensa área cicatricial que ha agrupado varios espacios porta. Material de autopsia.

En algunos pseudolóbulos había degeneración grasa moderada, pero en los nódulos de hiperplasia la esteatosis era nula.

Otro de los casos era una cirrosis, pero fue imposible clasificarlo dentro de los tipos antes descritos debido a lo exiguo del fragmento de la punción.

#### DISCUSION

Del total de casos reunidos (157 casos), excluyendo las cirrosis de tipo biliar por malformación congénita de las vías biliares, el 9.3% correspondía a todas las otras formas de cirrosis, lo cual demuestra una incidencia bastante alta.

Creemos haber podido seguir con punciones biopsias en serie en algunos pacientes y por comparación de los hallazgos histológicos en casos diferentes, los cambios morfológicos sucesivos en el curso evolutivo de algunas formas de hepatitis viral, que no curaron dentro de un período normal adoptando una evolución crónica y en las cuales la destrucción del tejido, la regeneración de este y el proceso de cicatrización condujeron finalmente a la cirrosis.

Los casos de hepatitis viral formaban el 14% del total del material examinado. A las cirrosis del tipo post-hepatitis correspondía el 57.1% de las cirrosis (excepto cirrosis biliar) y eran por tanto las más frecuentes en nuestra serie.

Los diversos grados de desnutrición formaban el bulto de nuestro material. Sólo en los casos de desnutrición grave (Kwashiorkor o estados marasmáticos) pudieron observarse cambios bastante característicos. En algunos de ellos se encontró fibrosis portal y cirrosis inicial.

Pensamos que los tipos portal y post-necrótico son en realidad verdaderas formas de cirrosis nutricional. De ciertas formas de cirrosis portal derivan por transformaciones sucesivas de necrosis y regeneración en cirrosis post-necróticas.<sup>23</sup> En otras ocasiones las cirrosis post-necrótica tendrían su origen en formas graves de hepatitis viral en las cuales ha habido gran destrucción del parenquima hepático, como en la llamada "atrofia amarilla sub-aguda del hígado".

A la cirrosis de tipo portal correspondía el 14.2% y a la del tipo post-necrótico el 21.4% de los casos de cirrosis. A cirrosis no clasificadas el 7.1%. Este último grupo representaba el segundo en importancia y consideramos que el factor etiológico más prominente era la desnutrición. Hemos observado que las cirrosis en los niños de nuestro país son casi idénticas a las de los adultos, sin haber podido encontrar diferencias específicas. No se encontraron las formas de cirrosis descritas en los niños de otros países como la Enfermedad veno-oclusiva de Jamaica. Sin embargo los casos de hepatitis crónica y cirrosis post-hepatitis tenían parecido

clínicamente a la cirrosis de los niños indíos, la cual también es atribuída por algunos autores a hepatitis viral.

Los cambios observados en los hígados de pacientes con Kwashiorkor eran idénticos a los descritos en África y otras regiones de Latino-américa. Las cirrosis post-necróticas parecían similares a las descritas en los adultos jóvenes de África pertenecientes a la tribu Bantu.

#### RESUMEN

Se estudiaron las secciones de hígado de 157 casos correspondientes a 75 autopsias y 82 biopsias. De estos se seleccionaron las entidades reconocidas como capaces de producir cirrosis y las cirrosis hepáticas. El material fue clasificado y las cirrosis según su tipo. La incidencia de cirrosis hepática en niños fue de 9.3%, excluyendo cirrosis biliar congénita.

El autor de este trabajo trató de demostrar la transformación por etapas sucesivas de hepatitis crónica en cirrosis post-hepatitis, observada a través de punciones en serie. La forma más frecuente de cirrosis fue la post-hepatitis 57.1% de las cirrosis, luego la cirrosis post-necrótica 21.4% y la portal con 14.2%. A las cirrosis no clasificadas correspondió el 7.1%. Se hicieron comparaciones con las cirrosis infantiles de otros países y se concluyó que los factores principales en la etiología de las cirrosis en Santo Domingo son posiblemente la Hepatitis viral y la Desnutrición.

#### SUMMARY

The liver sections of 157 cases, 75 autopsies and 82 biopsies were studied. From these, entities known to produce cirrhosis and cirrhosis of the liver were selected. The material was classified as well as the cirrhosis according to type.

The incidence of hepatic cirrhosis in children was 9.3%, congenital biliary cirrhosis were excluded.

The author of this paper tries to demonstrate transformation by stages through serial needle puncture biopsies of chronic viral hepatitis into post-hepatic cirrhosis.

The most frequent type of cirrhosis found was the post-hepatitic 57.1%, followed by the post-necrotic 21.4% and portal cirrhosis 14.2%. Non classified cirrhosis was 7.1%.

Our cases were compared with childhood cirrhosis in other geographical areas and it was concluded that the principal factors involved in the ethiology of childhood cirrhosis in Santo Domingo are most probably viral hepatitis and undernutrition.

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## RADIODIAGNOSIS\*

HERIBERTO PAGAN SAEZ, M.D.

### Case Summary (No. 5-63):

This 25 year old male developed progressive weakness of the left knee joint accompanied by pain. During the last six months pain increased in severity and was accompanied by increase in swelling and tenderness of the left knee.

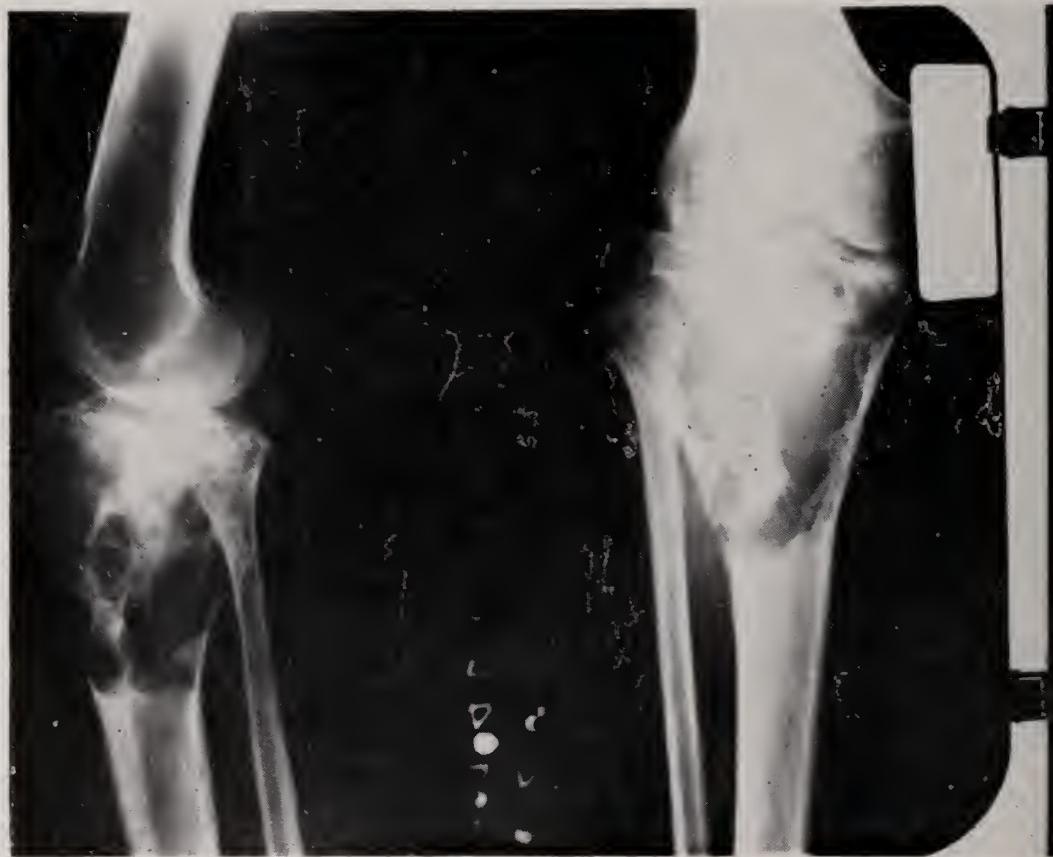


Fig. 5

### Interpretation:

A large osteolytic, trabeculated and expanding lesion in the proximal tibial metaphyseal-epiphyseal region is seen. There is

\* From the Department of Radiology, School of Medicine, School of Tropical Medicine, University of Puerto Rico, Rio Piedras, Puerto Rico.

scalloping of the corticalis internally with perforation in some sites. No intra-lesional calcification is observed.

**Diagnosis:**

Giant Cell Tumor or Osteoclastoma

True giant cell tumor or osteoclastoma is a bone tumor most often involving adults past the age of twenty (average age is thirty-two years). It usually appears following a history of trauma.

Histopathologically, there are numerous giant cells with spindle and round cells in the stroma.

Radiographically, it typically has a markedly radiolucent appearance with numerous trabeculae giving a "soap bubble" appearance. The lesion very often involves the epiphysis as well as the diaphysis, crossing the epiphyseal line, but this is not specific.

## LA LEGISLACION QUE HA REGULADO EL EJERCICIO DE LA PROFESION MEDICA EN PUERTO RICO: AYER Y HOY\*

JOSE MANUEL TORRES GOMEZ, M.D.\*\*

Aunque no es nuestra intención entrar en la historia detallada de las circunstancias que gobernaban el ejercicio de la Medicina en Puerto Rico desde sus comienzos más primitivos, creemos prudente hacer algunas anotaciones al efecto.

Los requisitos que tenía que llenar nuestro primer médico, el del pueblo indio, el "buhiti", eran algo distinto a los de ahora, pero existieron desde el primer momento. Si bien es verdad que estos "sacerdotes" solían siempre ser los más listos y charlatanes, y sobre todo, los más osados (no hubieran podido dominar a la masa del pueblo de otra manera), no es menos cierto que para "graduarse" tenían que sufrir un **ayuno** con plantas en los bosques hasta encontrarse con una fiera, y sobrevivir dicho encuentro. De ahí en adelante ejercían su magia al cuidado de los ya experimentados, ascendiendo en rango gradualmente, a medida que iban aprovechando las enseñanzas de los más sagaces. Requisito indispensable para poder demostrar al pueblo su profesión, era el ornamentarse de una manera exagerada y extravagante, con pinturas, pieles, plumas, huesos, etc. Este era el uniforme que los distinguía. Resulta curioso ver cómo se presta el hacer comparaciones, en algunos aspectos, con la situación que existe hoy, especialmente, cuando el llamado "buhiti" parece que estaba obligado a prestar los recursos de su inteligencia "a los caciques" más bien que a la comunidad. La ley que aparentemente existía entonces era que tenían que purgarse con el cacique, y que si el último moría, "los parientes y amigos del difunto solían sacarles los ojos, darles de palos, o aplicarles otros castigos". ¿Serían éstas las bases de donde evolucionarían las futuras relaciones entre médicos y alcaldes?

Llega el primer **Médico** a Puerto Rico, el Dr. Diego Alvarez Chanca, en el segundo viaje de Cristóbal Colón (19 de noviembre de 1493). Fue el primer médico oficialmente nombrado por un gobierno constituido (como lo era el español) que pisó nuestras playas, pero obviamente, nada había que reglamentar entonces.

Al entrar en años la colonia, poco a poco se fué reglamentan-

\* La mayor parte de lo descrito hasta principios del Siglo XX ha sido extractado del libro "Historia de la Medicina y Cirugía de Puerto Rico" cuyo autor fue Fundador y Primer Presidente de la Asociación Médica de Puerto Rico, el Dr. Manuel Quevedo Báez. La otra parte consiste de información obtenida de los archivos de nuestra Asociación y de las gestiones y experiencias personales del que suscribe.

\*\* Presidente Comité de Legislación - 1963.

do el ejercicio de la Medicina, y ya para el 1821 notamos que se hace referencia a un reglamento cuyo Capítulo 4 hasta señalaba cómo debía castigarse a aquél que ejercía sin título la profesión. Según el Decreto del 12 de mayo de 1797 expedido contra los intrusos en el ejercicio de la Cirugía, y el cual se mantuvo en vigor durante el régimen español, aquellos que ejercían sin el correspondiente título de médico-cirujano, cirujano, sangrador, o partera, sufrirían el siguiente castigo:

1. Convictos por primera vez — 50 ducados de multa;
2. Doble por la segunda, con destierro del pueblo de su residencia 10 leguas a la redonda;
3. Convictos por tercera vez — 200 ducados de multa, destinándolos a uno de los presidios de África o América.

Hoy día, debido a la condescendencia democrática y un falso sentido de liberalismo, nuestro sistema y nuestras leyes permiten que un individuo **convicto cinco (5) veces** ante las Cortes de Justicia por la práctica ilegal de la medicina, siga ejerciendo la profesión en San Juan sin la correspondiente licencia, en abierto desafío de nuestro Gobierno. Como el llevar a cabo esa práctica ilegal no le va a costar más que cien dólares de multa si es acusado y convicto de nuevo, es fácil de explicar por qué dicho sujeto le ha perdido el respeto a nuestra manera de hacer justicia.

Otra Real Orden del 1827 dictaba, entre otras cosas, “que el depósito, así como el importe de los demás gastos precisos para obtener cualquier grado en la profesión, se efectuará antes de procederse a los exámenes correspondientes. Y dispone además, que si fuese el aspirante reprobado, perderá el depósito que hubiere hecho”. Es interesante el que hoy, 136 años más tarde, se encuentren estas disposiciones todavía en vigor.

No fue hasta el 28 de febrero de 1839 que, por Real Decreto del Gobierno de España, se estableció el primer Tribunal Médico que funcionó en Puerto Rico. Creando un organismo que tuviese control de todas las actividades médicas que se desarrollasen en la Isla, se esperaba poner coto a la corrupción y abusos que existían en cuanto a prácticas médicas fraudulentas (que no eran pocas). A este organismo se le dió el nombre de Real Subdelegación de Medicina y Cirugía, y comenzó a funcionar en el año 1841. Dicha Junta habría de ser constituida por tres profesores médico-cirujanos y un secretario, cargos honoríficos, como lo son hoy. Habría también de redactar un reglamento, fijando el importe que debían abonar los individuos que aspirasen a tomar los correspondientes exámenes, no sin antes presentar aquellos créditos que le dieran derecho al ejercicio de la profesión médica en la Isla. La Subdelegación tenía también la encomienda de revalidar títulos procedentes de **universidades extranjeras**. A la vez, podía conceder licencias, **previo examen**, de médicos prácticos, a los cuales se les fa-

cultaba para tratar las enfermedades externas y mixtas, pero no las internas y puramente médicas.

La citada Real Orden autorizaba a la Junta a tener por válidos para ejercer la medicina en Puerto Rico, los títulos exhibidos ante la Autoridad Superior de la Isla y librados por la Junta Superior de Medicina y Cirugía de Cuba, hasta el día en que la de Puerto Rico comenzara a funcionar. Tenía la Subdelegación también carácter consultivo para dar luz al Gobierno e intervenir en todas aquellas cuestiones relacionadas con la Medicina que plantearan los Tribunales de Justicia.

También ofreció exámenes a aquellos individuos que con carácter y funciones de curiosos, se dedicaban al arte de curar. Si los aprobaban ante la Subdelegación, el Gobierno de la Isla les expedía la autorización correspondiente. Sin embargo, y esto que lo oiga nuestra Legislatura y nuestro presente Tribunal Examinador de Médicos, a los ocho años de estarlos celebrando, la Junta los descontinuó por considerarlos inútiles, ya que no remediaban la necesidad sentida de un personal facultativo idóneo, ni ponían fin a los abusos y prejuicios que imperaban. Esto me hace recordar cuando, en el año 1955, nuestro Tribunal Examinador de Médicos descontinuó los exámenes especiales que se venían ofreciendo desde el 1943 a los candidatos que ejercían al amparo de leyes de privilegio por casi iguales motivos. ¡Cómo se repite la historia!

Algunas funciones de provecho que llevó a cabo la Junta son las siguientes:

1. Organizó y reglamentó el Cuerpo de Médicos Titulares "con la aprobación y beneplácito del gobierno superior". En 1849, con objeto de mejorar la Beneficencia Municipal, estableció los requisitos para poder desempeñar el cargo de Médico Municipal, los cuales exigían poseer el título académico de licenciado en Medicina y Cirugía, acreditar probada conducta moral y política, no desempeñar otro cargo público relacionado con la profesión, tener nueve años de práctica y previa oposición. Ese servicio de Médicos Titulares fue siempre, entonces lo mismo que en los últimos tiempos, deficiente, y en sus resultados, casi infructuoso. ¿Por qué? Sencillamente, porque "en los municipios, ese servidor público no solo estuvo mal y depresivamente retribuido, sino que hubo de prestarse a veces, sumiso y obligado, a imposiciones mañasas e imperativas de aquellos alcaldes autoritarios o con ribetes de casi-ques a la usanza de aquellos tiempos. La mayoría de los enfermos pobres, más que el auxilio de los medicamentos, lo que requerían era alimentación y cama. Fue así, las más de las veces, un servidor político, instrumento de caprichosos mandatos, más que médico y guardador de la salud del pueblo." Esta cita que se refiere a las condiciones existentes en el Siglo XIX, muy bien podría aplicarse al Siglo XX. Y si no, ¡que se lo pregunten a nuestros

médicos que acaban de trabajar como Directores de Beneficencia Pública!

2. Impuso cuarentena a los barcos procedentes de puertos infestados.

3. Estableció que cada municipalidad debía de tener un médico o más para funciones de beneficencia pública, según sus necesidades, costeándolos de sus mismos fondos. **Independientemente**, ese médico podía prestar servicios, previa remuneración, a los enfermos de condición económica solvente. ¿Qué les parece ésto a nuestros "modernos" oficiales de gobierno que interesan que todos, indigentes y solventes, vayan a obtener servicios gratuitos a los dispensarios y hospitales públicos?

4. Hizo el papel de Comité de Mediación y Querellas atendiendo reclamaciones de pacientes.

5. Fué consultiva en asuntos de cementerios, acueductos, construcción de hospitales, epidemias, problemas médico-legales, y en ramos de higiene pública. ¡Vaya meritoria labor!

En 1820, el Dr. José Espaillat fundó una "Sociedad Médica" para instruir en las carreras de Medicina y Farmacia. Hubo que suprimirla más tarde debido a la falta de profesores y a otras dificultades de funcionamiento, no sin antes graduar al primer médico puertorriqueño, el Dr. Emigdio Antigue. En su lugar, en el 1845, se fundó una Escuela de Cirujanos o Médicos Prácticos no verdaderamente científica, pero lo suficiente práctica para mejor atender las necesidades de los enfermos.

Ya en el 1838 se hizo compulsorio el Registro de Médicos.

Otra nota interesante es la Real Orden del 17 de junio de 1846, la cual en uno de sus apartados dice "que ningún profesor de medicina o de cirugía podrá entrometerse a visitar enfermo alguno que se halle a cargo de otro profesor, a no ser de acuerdo con éste, o que fuera elegido por los interesados, y después de haberse enterado del estado del paciente por medio de una junta o consulta. Si así aconteciere, el **intruso** será reconvenido y castigado por la autoridad, siempre que aparezca cierta la queja o manifestación que se hiciere". Aquí ya se ponían en práctica los principios de la ética médica **por ley** aunque todavía no había unidad de cuerpo médico verdaderamente organizado. Vale la pena meditar sobre el hecho de que hoy, habiendo ese cuerpo, que es la Asociación Médica de Puerto Rico, se siguen imponiendo leyes, que, si proponérselo, estimulan y permiten prácticas totalmente reñidas con la ética que gobierna nuestra profesión.

En una circular del 10 de julio de 1846 son toleradas las mujeres que ejercen el ramo de "Obstetricia" en vista de la falta absoluta de ese tipo de personal médico que hasta aquella fecha hubo en el país. Cinco días más tarde se autorizaba a determinadas mujeres de la vecindad a ser prácticas de parteras (com-

dronas), pero que únicamente podían asistir a los partos naturales o normales, absteniéndose de recetar y hasta de aconsejar medicamento interno de clase alguna. La Subdelegación recomienda a que se establecieran turnos de servicio, y que éstos se publicaran en los periódicos para beneficio de la comunidad.

Para el 1847 se sentía la necesidad de una organización médica, además de la Subdelegación, que estableciera normas serias y formales de conducta, que contribuyera a garantizar la salud pública, y que velara por los altos intereses de la sociedad. Curiosos intervenían en casos de autopsias y hasta eran encomendados a prestar los servicios de vacunación. Había facultativos llamados de tercera clase que, por no decir más, se excedían en sus funciones.

Una nota con la cual estamos familiarizados, es la que dice que el Gobierno en 1849 redujo los gastos de la Junta. Digo familiarizados, porque yo palpé en la década del 1950, los limitados recursos que por un escaso presupuesto, tenía nuestro Tribunal Examinador de Médicos a su disposición. Esto parece un mal crónico de los gobiernos que, aparentemente, no se tiene gran interés en corregir, quizás por no dársele la debida importancia que merecen las responsabilidades de este organismo gubernamental.

En febrero 15 de 1851, la Subdelegación condena la inserción de anuncios y polémicas sobre asuntos médicos en los periódicos. ¡Cuál sería su reacción a lo que se publica hoy!

En el 1855, por el término de un año, y debido a la falta de facultativos en la Isla, se dispone otra vez admitir a exámenes ante la Subdelegación a aquellos con "algunos conocimientos teórico-prácticos en cirugía-médica" que estaban interesados en recibir el título necesario. Vale la pena apuntar aquí que no se hace referencia alguna a exámenes especiales. Lo que se rebajaba por el término de un año eran los requisitos a admisión para examen. Sin embargo, parece que esto tampoco resolvió el problema, ya que lo que hacía falta en la comunidad era conocimientos en los practicantes y no simplemente títulos. Como resultado de esta política reinó la confusión, pues llegó a haber gran diversidad de títulos, al igual que en nuestros días con la gran diversidad de licencias provisionales. ¡Parece que el hombre sólo quiere aprender a través de su propia experiencia!

Para el 1856 aumentaban las irregularidades en los servicios médicos debido a la intromisión de los curiosos en el ejercicio de la medicina. Aunque la Subdelegación había querido organizar dichos servicios estableciendo responsabilidades a través de un Reglamento, esto no le fué posible, ya que el Gobierno Superior (¡Vieja historia!) todavía no lo había aprobado. Por fin, en el año 1858, el Gobierno prohíbe todo ejercicio a aquellos que no han revalidado mediante exámenes.

En el 1859, debido a los pocos médicos con experiencia que querían trabajar en los municipios, la Subdelegación redujo el requisito de años de práctica que se exigía para ese puesto de nueve a dos. Sin embargo, esta modificación no atrajo a muchos ya que la causa fundamental de su alejamiento (condiciones inaceptables de trabajo) no se había resuelto. De hecho, cuando en el 1860 el Gobierno pidió se le aconsejara en cuanto a la mejor forma "de obligar a los pueblos" a tener médicos titulares, la Subdelegación le contestó que dotando las plazas de tal modo que ofrecieran ventajas sobre las que ya tenían los médicos. Esta contestación todavía se puede aplicar a los problemas actuales de beneficencia.

El 29 de mayo de 1866 se publicaron los requisitos que se iban a exigir a los practicantes de Cirugía Menor, Ministrantes o Flebotomianos. Ellos fueron finalmente aprobados el 4 de noviembre y consistían en:

1. Haber cumplido 20 años de edad y presentar créditos de buena conducta.
2. Práctica de tres años en Hospital o con Facultativo, previa matrícula en la Subdelegación cada año, haciendo constar dónde y con quién hace la práctica.
3. Al término de los tres años tiene que sufrir un examen teórico-práctico sobre conocimientos de la Cirugía Menor y abonar 250 pesetas.
4. Se les expedía una certificación como título, después que aprobaran dicho examen, firmada por el Presidente y el Secretario.
5. Los desaprobados podían volver a presentarse a los seis meses, y si no eran aprobados la segunda vez, se les concedían otros seis meses, siendo este tercer examen su última oportunidad. Los que no cumplían con estas disposiciones eran considerados como intrusos sujetos a las penas establecidas por las leyes.

Como ustedes pueden ver, más se le exigía a un flebotomiano para poder ejercer en el Siglo XIX que a un médico bajo la Ley #4 de septiembre de 1961 en el Siglo XX.

Más tarde, en 1857, se establecen requisitos para que estos practicantes pudieran aspirar al título de Facultativos de Segunda Clase, según estaba vigente en España. También, en el mismo año, la Subdelegación sentó el principio de que la **profesión médica es libre** por estar reconocida por el Gobierno y que, por lo tanto, el médico no tiene obligación de desempeñar otros cargos que aquellos que voluntariamente él se imponga. Obviamente, hoy día se ha dado un paso atrás, ya que la legislación vigente obliga a un

médico (extranjero) a trabajar en determinada plaza del Gobierno, so pena de no poder trabajar como médico en el país.

A pesar de todos los esfuerzos de la Subdelegación, ésta se queja en 1868, de ser un organismo inválido ya que no se estaba aplicando la Ley Orgánica de Sanidad que regía en España. La vigilancia sobre el ejercicio de las profesiones estaba en manos de los corregidores y los alcaldes, y éstos no parecían ser muy estrictos con los intrusos. Se redactó entonces un reglamento mediante el cual el Gobierno Superior Civil nombraba médicos **Coadjutores** en cada Departamento de la Isla a propuesta de la Subdelegación. Este era un cargo honorífico y se consideraba como un mérito en su carrera. Estos coadjutores eran responsables de velar por el cumplimiento de las leyes, reglamentos, circulares, etc., examinar los títulos de los que ejercían, dar parte de las infracciones, formar la estadística médica de la Isla, etc. Viene esto a ser, más o menos, la base de donde más tarde nace la relación hoy existente entre el Tribunal Examinador de Médicos y el Departamento de Justicia, relación que sobre el papel parece ser la solución para perseguir y castigar al que ejerce ilegalmente la Medicina en nuestro país, pero que en la práctica deja mucho que desear. Sigue hoy el Tribunal con grandes obstáculos y dificultades para poder llevar a cabo esa misión, pues la ayuda que le brinda el Departamento de Justicia no ha tenido la efectividad esperada en un gran número de los casos. La mayoría de nuestros alcaldes también han contribuído durante las últimas dos décadas, al igual que entonces, a permitir prácticas ilegales, haciéndose de la vista larga cuando los médicos que sólamente estaban autorizados para trabajar en la plaza de la Beneficencia Municipal, ejercían la práctica privada de la profesión sin la licencia correspondiente.

En 1875 la Subdelegación creó la profesión de Parteras, y al año siguiente estableció el reglamento que las regulaba. Se tenían que someter a un examen y aprobarlo antes de poder ejercer. Los otros requisitos que se exigían eran similares a los que se exigían a los practicantes.

En 1883 se estableció el Colegio Central de Medicina para remediar el mal de carencia de personal médico y para exigir, una vez más, a los intrusos sin título, que sufrieran los correspondientes exámenes so pena de ser multados. En 1888, el Colegio se convirtió en Cátedra de Medicina (en el Ateneo) al crearse la "Institución de Enseñanza Superior" bajo jurisdicción de la Universidad de la Habana. Una Comisión de Catedráticos se trasladaba a San Juan cada año para llevar a cabo los exámenes. Así se entrenaron varios estudiantes en el primer año de Medicina que luego siguieron sus estudios en universidades americanas. Sin embargo, este otro esfuerzo de enseñanza universitaria duró sólo hasta el año 1893.

## Dominación Americana

En el 27 de febrero de 1899, poco tiempo después de implantarse el gobierno americano, el Secretario de Estado solicitó de la Subdelegación lo aceptado en cuanto a la práctica de la Medicina en Puerto Rico. La Junta contesta que todos los individuos que poseen títulos universitarios nacionales fueron admitidos al libre ejercicio de la profesión. Los ciudadanos nacionales con títulos de universidades extranjeras habían sido autorizados para la práctica mediante un examen, con la diferencia de que no podían ejercer cargos públicos excepto en ausencia absoluta de un poseedor de título nacional para la plaza en cuestión. Y si alguna vez lo llegaran a ejercer por esa razón, caducarían sus derechos al ser pedida la plaza por un título nacional. Además, los ciudadanos extranjeros, aún con títulos revalidados, nunca podían desempeñar cargo público alguno, dedicándose sólo al ejercicio privado de la profesión. Es decir, que entonces se exigía el mejor médico, el título nacional, para la Beneficencia, y del que se tenía dudas, que tratara al paciente. La disposición de nuestra actual Legislatura ha sido que al extranjero que no ha revalidado se le reserva para trabajar en cargos públicos solamente. ¡Qué contraste!

En ese mismo año la Secretaría de Justicia se creyó autorizada para ella sola reconocer y expedir títulos de Cirujano-Dentista. La Subdelegación se sintió ofendida por tal orden y se quejó de inmediato a la autoridad correspondiente. La orden quedó sin efecto cuando, por resolución de la Secretaría de Estado, se le restituyeron todos los derechos a la Subdelegación, quedando así la autoridad para clasificar dichos profesionales en el organismo al cual verdaderamente le corresponde. Sin embargo, este concepto no fue siempre respetado de ahí en adelante. Leyes de privilegio fueron sucesivamente aprobadas por nuestros legisladores en los años '11, '19, '42, '43, '46, '61, '62, y '63. Por ejemplo, la Ley #4 del 1961 autorizó al Secretario de Salud a tomarse él solo, la prerrogativa de determinar quién podía trabajar como médico en Puerto Rico sin examen de reválida.

La Subdelegación de Medicina cesó en sus funciones el 29 de junio de 1899. La suplantó una Junta Superior de Sanidad, y ésta, el 30 de abril de 1900 y por disposición de una Orden General, fue traspasada al Departamento del Interior. En esa misma fecha se creó el "Board of Health", también bajo la dirección de ese Departamento. Fué a este organismo al que correspondió llevar a cabo los exámenes de reválida el 11 de junio del mismo año. Se examinaron 5 médicos, 8 farmacéuticos, 5 practicantes, 2 Cirujanos Dentales, y una enfermera. Fueron reprobados 3 farmacéuticos, y un practicante. Una segunda convocatoria se llevó a efecto para enero de 1901.

El 21 de septiembre de 1902 se funda la Asociación Médica de Puerto Rico (AMPR) bajo la presidencia e iniciativa del Dr. Manuel Quevedo Báez. Y el 12 de marzo de 1903, a instancias de la A.M.P.R., la Legislatura crea el Board of Medical Examiners (hoy Tribunal Examinador de Médicos) sucediendo así al Board of Health.

No tardaron tiempo los directores de la A.M.P.R. (3 de marzo de 1904) en solicitar la independencia del Oficial de Sanidad (médico) de la jurisdicción del municipio para pasarlo al Departamento de Sanidad. Las quejas por las imposiciones de los alcaldes reclamaban este cambio.

El 12 de marzo de 1908 se aprueba la ley que establece que "los médicos, en ejercicio en Puerto Rico, cuando sean requeridos por los Tribunales de Justicia . . . serán considerados como **expertos . . .**" Esta ley se justificaba entonces. Sin embargo, hoy se debe enmendar más de lo que ha sido, debido a los avances de la medicina y cirugía. El campo de la medicina es tan amplio que no hay médico que se pueda llegar a considerar experto en todas las ramas de la profesión. Esa consideración debe limitarse al especialista certificado en determinado aspecto. Sólo así se podrá hacer la mejor justicia.

El combatir leyes de privilegio personal relacionadas con el ejercicio de la medicina no es nada nuevo. En el 1911, el Tribunal Examinador de Médicos así lo hizo a través de su Presidente, el Dr. E. J. Saldaña, cuando se permitió a doctores con cinco años de práctica anteriores a la creación del "Board", ejercer por **fiat legislativo**, sin examen. Los legisladores no estuvieron de acuerdo con la posición adoptada por el Tribunal, y aprobaron la Ley Núm. 79 de ese año. La ley Núm. 43 del 1919 fue el resultado de otro privilegio legislativo de carácter similar.

La ley que creó al Tribunal en el 1903 fue enmendada repetidas veces en los años '06, '13, '15, afectando su organización y funcionamiento, y finalmente derogada por la #73 en el 1923, que establece una nueva Junta. Esta última vuelve a ser enmendada en los años '24, '25, '27 y '28. Parece que resultaba difícil establecer por ley lo que, de una manera precisa, se quería conseguir. En el 1930, se legisló para reglamentar la práctica de la Optometría por separado. Y finalmente en el 1931 se aprueba la Ley #22 que viene a ser la fundamental en cuanto al ejercicio de la profesión médica en la Isla. Esta es la que establece todos los requisitos que se necesitan para poder solicitar la reválida, y también, lo que se requiere para poder ejercer la medicina dentro de ley. Varias veces enmendada, la Ley #22 continúa siendo la básica que regula nuestra profesión, aunque, como verán más adelante, nuestra legislatura la deja sin efecto temporalmente (sin derogarla) mediante leyes de privilegio para favorecer determinados grupos. Esto re-

sulta paradójico, ya que la Ley #22 se aprobó con la intención de acabar con todos los privilegios, los intrusos, y los fiat legislativos concernientes a la práctica de la medicina en Puerto Rico. De hecho, se aprobó legislación adicional en los años '35, '38, y '39 haciendo más rígido su contenido.

Después que a través de todos estos años de lucha finalmente se consigue la implantación de legislación adecuada que le asegura al pueblo un médico garantizado, aparece en escena la Segunda Guerra Mundial. Comienza el reclutamiento de médicos y la población civil siente la escasez de ese profesional en todos los países envueltos en ella. En Puerto Rico, el Gobierno, tratando de conjurar la crisis, decide hacer algo por aumentar el número de médicos en el país. Principian a surgir leyes que aún llevando un buen propósito terminan en una mala práctica debido al camino equivocado que se siguió. Las Núm. 26 y Núm. 13 del 1942, y la Núm. 29 del 1943 autorizaron a ciertos médicos, que no llenaban los requisitos bajo la Ley básica (22), a ejercer en la Isla sin que se los exigieran. Volvimos a los desatinos de antes y no valió la oposición de la AMPR. Otra ley, la #304 del 1945, enmienda la Ley regular (22) con el mismo fin. Quizás el cambio más importante es que se comienza a exigir al médico que termina el internado a que practique por un período mínimo de un año en un municipio de segunda o tercera categoría mediante licencia especial, indicando el pueblo donde habrá de llevarse a cabo dicha práctica. Sólo después de haber cumplido con este requisito es que se le permite tomar la segunda parte de la reválida, y de aprobar ésta, recibir la licencia regular y permanente. Esta medida, justificada en aquel entonces, viene a ser más tarde, cuando ya no era necesaria, responsable de grandes abusos al utilizarse como medio que ha permitido el ejercicio de la profesión hasta a individuos que repetidas veces fracasaron en el examen de reválida. Esta enmienda todavía se encuentra en vigor.

En el 1946 se aprueba la Ley #383 por medio de la cual se inicia la contratación de médicos extranjeros. Esta ley es el resultado de la presión ejercida por la mayoría de los alcaldes, quienes, quizás inconscientemente, dejándose llevar más por las necesidades políticas que las médicas, piden médicos sin importar mucho sus quilates como tales. Y aquí comienza a tergiversarse la posición adoptada por la AMPR. La Asociación se opuso a la contratación de "cualquier" médico extranjero". Sostuvo siempre la AMPR que el médico que se fuera a traer a Puerto Rico debería de ser del calibre y la categoría académica de los médicos puertorriqueños que estaban en el ejercicio de la profesión. Solamente así se podía mantener el alto nivel en la práctica de la medicina que a esa fecha el médico puertorriqueño había conseguido a través de grandes esfuerzos, estudios, y sacrificios. Y esta sana po-

sición, que primordialmente va en defensa y protección de la salud de nuestro pueblo, se interpreta (y a veces he pensado que maliciosamente) como que la AMPR no quiere que se importe médico alguno.

Comienzan a llegar los médicos contratados al amparo de esa ley, y sucede lo que tenía que suceder. La inmensa mayoría de ellos no podían aprobar los exámenes **usuales** que ofrecía el Tribunal Examinador. Esto finalmente condujo a la indeseable práctica de tener que ofrecer exámenes especiales a estos candidatos. Mientras uno de los nuestros tenía que contestar 10 preguntas, otro sentado a su lado, por el mero hecho de ser extranjero, no tenía que contestar más que cinco, en el mismo examen. Pero como estas normas, aunque rebajadas, todavía constituyan un obstáculo, se decide finalmente ofrecer a estos candidatos exámenes orales especiales llevados a cabo individualmente por los miembros del Tribunal. Aquí nos topamos con el **poco saludable** estado de un funcionario público, específicamente el Comisionado de Sanidad entonces, y el Secretario de Salud ahora, ser autorizado por ley como **único** examinador y contratante a la vez, violando uno de los principios básicos sobre los que descansa la buena marcha de nuestra sociedad, al actuar como juez y como parte.

Esta situación se prorroga con ligeras modificaciones por medio de las leyes Núm. 437 del '47, Núm. 6 del '48, Núm. 218 del '50, Núm. 34 del '54, y Núm. 51 del '55. Durante esta época se aprueban también las leyes Núm. 320 del '46, Núm. 40 del '50, y Núm. 6 del '52 que modifican la composición del Tribunal Examinador y se establece un nuevo registro de médicos. Para el 15 de mayo de 1952 se aprueba la Ley Núm. 493 reconociendo la profesión de la Quiropráctica y estableciendo su propia Junta Examinadora. La AMPR combatió esa ley entonces porque se prestaba y todavía se presta para que ese grupo lleve a cabo ciertas prácticas que son y deben ser atributos del médico solamente, ya que éste es el que las ha estudiado en toda su profundidad. De hecho, esto ha causado una gran confusión en los enfermos ya que muchos de ellos han ido a tratarse con el "Doctor" (Quiropráctico) en la creencia de que es un médico.

El 24 de mayo de 1957 se aprueba la Ley #53 que, aunque prorroga la #383 un año más, le retira el poder de contratación a todos los funcionarios públicos con excepción del Gobernador. Al año siguiente se aprueba la Ley #75 que deroga la 383 y se termina con la importación de médicos reconociendo así nuestra Legislatura que no existía escasez de médicos en Puerto Rico que exigiera tal legislación. A la vez se sentaban las bases que permitían al médico extranjero que vino a Puerto Rico al amparo de estas leyes especiales, conseguir la licencia regular y permanente sin perder su ciudadanía. Requisito indispensable era el de apro-

bar los exámenes regulares que ofrecía el Tribunal. Un número exiguo de médicos extranjeros así lo hicieron, y hoy día no sólo gozan de la licencia que les permite el libre ejercicio de la profesión en Puerto Rico sino que también han sido aceptados como miembros en la AMPR.

En ese mismo año (1958), se aprobó la Ley #61 que enmendó la Ley básica (22). Esta enmienda vino a corregir un gran defecto del cual adolecía nuestra ley básica. Al decir que los solicitantes deberán "haber aprobado no menos de dos años de bachillerato en un colegio en el cual se enseñen ampliamente, entre otras materias, las de química orgánica e inorgánica, física superior . . ." la ley no especificaba que el candidato tenía que aprobar dichas asignaturas. Al exigir el Tribunal dicha aprobación, varios solicitantes apelaron a las Cortes de Justicia. Estas últimas le negaron la razón al Tribunal y hubo que conceder licencias regulares para ejercer la profesión en nuestra Isla hasta a médicos que habían fracasado en dichas asignaturas. La enmienda aprobada corrigió ese defecto ya que específicamente exigía la aprobación de cada asignatura en particular.

En el 1950 se creó la Escuela de Medicina. Sacó a relucir esto porque una de las razones que se dieron para justificar su creación, fue la escasez de médicos que había en Puerto Rico. Sin embargo no satisfechos con los médicos que ha producido, se continúa legislando para seguir importando médicos extranjeros, permitiéndoles ejercer hasta sin dar pruebas de su capacitación. Traigo el punto de la Escuela además, porque también se dijo que la AMPR estuvo opuesta a su creación. Esta impresión absolutamente falsa todavía reina en el pensamiento de algunos pocos amigos de nuestra Asociación. Quiero aprovechar esta oportunidad para señalar que la AMPR **nunca** estuvo opuesta, y por el contrario, se expresó siempre en favor de la creación de una Escuela de medicina. Sostuvimos que no debiera ser una escuela para formar profesionales de dudosa capacidad, porque creamos que no debe haber servicios profesionales distintos para los diferentes sectores de la población de Puerto Rico. Esto se dijo tan temprano como en el 1942. En abril del 1944, nuestra Cámara de Delegados se expresó oficialmente a favor de su establecimiento. Si no se creó una Escuela de Medicina entonces no fue por culpa de la AMPR. Son muchos los documentos que existen que confirman esa actitud, pero este no es el momento para entrar en esos detalles. Que baste con señalar que a lo que se opuso la AMPR fue a que la Fundación Paderewski fuera usada como núcleo alrededor del cual se creara la Escuela de Medicina. Esto ocurrió en el 1948. Se pretendió hacer ver al público que la Asociación se oponía a la creación de una Escuela de Medicina en Puerto Rico, cuando lo que se deseaba era que no se fuera a esta-

blecer de la noche a la mañana, una Escuela que no reuniese los requisitos de una debidamente reconocida. Información solicitada de las autoridades médicas en Londres y Edimburgo en cuanto a la preparación de los hombres que integraban la facultad de la Escuela propuesta, corroboraron nuestras sospechas. Las autoridades universitarias, al corroborarlas también independientemente, finalmente desistieron de ello, justificándose así nuestra oposición en aquella época.

Volviendo a la historia de la legislación que siguió gobernando el ejercicio de la profesión médica en nuestra Isla después del 1958, llegamos al año 1961.

Con el endoso del Tribunal Examinador de Médicos se aprueba, en junio, la Ley #97 que reconoce la Podiatría como profesión, la separa de la Ley 22 y le permite establecer su propia Junta Examinadora. Ya no se exige ser médico para poder ser podíátra como lo exigía la Ley 22.

Esta también es la época del exilio cubano y llegan a nuestras playas nuestros colegas cubanos. La clase médica de Puerto Rico, por mediación de su Asociación, en un gesto genuino y sincero, propio de hermanos en Cristo, propone legislación permitiéndoles el libre ejercicio de la profesión sin tener que sacrificar su ciudadanía, pero como es natural, exigiendo la prueba de capacitación completa, tal como había sido sugerido por la Directiva de la Asociación de Médicos Exiliados Cubanos en carta que se nos dirigiera. Gran sorpresa fué para nosotros el ver que la legislación presentada, finalmente aprobada, y no objetada ni por el Secretario de Salud ni por los médicos cubanos, no exigía prueba de capacitación **alguna** antes que éstos pudieran ejercer. Además, esa legislación los obligaba y los limitaba a trabajar sólo con el Gobierno. De hecho, se autorizaba al Secretario de Salud a emplear como médicos a individuos que lo convencieran de que eran médicos con sólo alguien testificarlo, gozando así de todos los atributos que correspondían al Tribunal Examinador. Esta fué la célebre Ley #4 que se aprobó por encima de la oposición de la Asociación Médica de Puerto Rico el 27 de septiembre de 1961.

Esta ley se enmienda el 26 de junio de 1962 por la #107 que limita el examen a tomarse más tarde a "la parte correspondiente a las Ciencias Clínicas". De nuevo la AMPR vuelve a oponerse a otra medida que adulteraba aún más el ejercicio de nuestra profesión. Ahora se trataba de una capacitación a medias. Se redactó un memorandum donde se enumeraron nuestras objeciones y se envió al senador H. Rivera Colón quien lo leyó en el "floor" pasando así al Diario de Sesiones del Senado el 21 de mayo. Las alegaciones de la AMPR no fueron aceptadas.

Estamos ya en el 1963 y siguen los médicos extranjeros ejerciendo en Puerto Rico sin examen de reválida. A pesar de sen-

satas objeciones levantadas por la AMPR, y apoyadas por un numeroso y consciente sector de nuestra población, el Gobernador, el 29 de junio, convirtió en ley, con su firma, el sustitutivo del P. de la C. 731. Esta autorizará a los médicos extranjeros contratados por el gobierno, a ejercer en Puerto Rico con sólo aprobar "medio" examen de reválida. Esperamos que esta medida equivocada tenga una vida corta y que pronto todo nuestro pueblo pueda volver a gozar de la tranquilidad de conservar su salud mediante el uso de un médico que ha sufrido los rigores, con éxito, de un examen de reválida completo.

**LEYES APROBADAS EN TORNO EJERCICIO PROFESION MEDICA  
DE PUERTO RICO**

1. 12 marzo 1903,	P. 124	Creó Junta de Médicos Examinadores
2. 1 febrero 1906,	P. 103	Enmienda a ley Junta
3. 9 marzo 1911,	Ley 79	Privilegio para ciertos médicos poder ejercer.
4. 13 marzo 1913,	" 28	Enmienda a ley Junta
5. 11 marzo 1915,	" 6	Enmienda a ley Junta
6. 7 junio 1919,	" 43	Otro privilegio por fiat legislativo para que ciertos médicos pudieran ejercer; no llenaban los requisitos de la Junta.
7. 30 julio 1923,	" 73	Establece nueva Junta; deroga todo lo anterior.
8. 1 julio 1924,	" 15	Enmienda a nueva Junta
9. 20 junio 1925,	" 37	Enmienda a nueva Junta
10. 13 mayo 1927,	" 45	Enmienda a nueva Junta
11. 19 abril 1928,	" 20	Enmienda a nueva Junta
12. 15 mayo 1930,	" 78	Reglamento Optometría por separado
13. 22 abril 1931,	" 22	Ley básica para acabar con todos los privilegios; sentó estrictos requisitos para examen.
14. 1 mayo 1935,	" 46	Enmienda a ley básica que la hacía más estricta
15. 6 mayo 1938,	" 96	Enmienda a ley básica que la hacía más estricta
16. 15 mayo 1939,	" 172	Enmienda a ley básica que la hacía más estricta
17. 10 abril 1942,	" 26	Privilegio para ciertos médicos poder ejercer.
18. 23 nov. 1942,	" 13	Privilegio para ciertos médicos poder ejercer.
19. 29 abril 1943,	" 29	Privilegio para ciertos médicos poder ejercer.
20. 15 mayo 1945,	" 304	Enmienda a ley básica; exige 1 año servicio municipios; origen licencias provisionales.
21. 13 abril 1946,	" 320	Enmienda a composición Tribunal Examinador (Junta)
22. 22 abril 1946,	" 383	Autoriza contratación médicos extranjeros
23. 14 mayo 1947,	" 437	Autoriza contratación médicos extranjeros

24.	19 agosto 1948,	"	6	Autoriza contratación médicos extranjeros
25.	10 abril 1950,	"	40	Nueva numeración y registro Lie. de médicos
26.	5 mayo 1950,	"	218	Autoriza contratación médicos extranjeros
27.	15 mayo 1952,	"	493	Establece, reglamenta, y reconoce la profesión de Quiropráctico; Junta por separado
28.	24 julio 1952,	"	6	Enmienda a composición Tribunal Examinador de Médicos
29.	18 mayo 1954,	"	34	Autoriza contratación médicos extranjeros
30.	2 junio 1955,	"	51	Autoriza contratación médicos extranjeros
31.	24 mayo 1957,	"	53	Sólo el Gobernador puede contratar médico extranjero
32.	20 junio 1958,	"	61	Enmienda a ley básica; exige 3 años pre-médica y aprobar asignaturas específicas.
33.	23 junio 1958,	"	75	Cesa toda importación médicos extranjeros
34.	21 junio 1961,	"	97	Establece, reglamenta, y reconoce la profesión de Podiatra; Junta por separado.
35.	27 sept. 1961,	"	4	Autoriza contratación médicos extranjeros sin examen.
36.	26 junio 1962,	"	107	Enmienda a la anterior; prórroga y medio examen.
37.	29 junio 1963,	"	96	Autoriza contratación médicos extranjeros vía aprobación medio examen.

Gobernador crea Comisión Consultiva sobre problemas médicos;

(el Presidente de la AMPR es 1 de 16 miembros)

## SECCION DE RESUMENES

**PREVENTION OF THROMBOSIS IN THE INFERIOR VENA CAVA** (Preven-ción de la trombosis en la vena cava inferior), Just Viera, J. O. y G. H. Yeager. Departamento de Cirugía, Facultad de Medicina de la Universidad de Maryland, Surg., Gynec. & Obst. 117: 3: 271 (Septiembre, 1963).

Los autores estudiaron, en la vena cava inferior de perros, el efecto trombótico de estasis y traumatismo, así como la acción antitrombótica de un dextrán cuyo peso molecular era de 75,000.

Juzgan que los resultados son alentadores: el dextrán de bajo peso molecular —pariente de la heparina— tiene acción antitrombótica, pero dónde radica, aún no se sabe. Quizá cubra la capa interior del segmento vascular traumatizado, modifique así la corriente de lesión y prevenga la trombosis. Hay en este artículo interesantes comentarios sobre las cualidades anticoagulantes del dextrán, cualidades que podrían colocarlo en las primeras filas de nuestro armamento terapéutico, dentro y fuera de la cirugía.

MANUEL E. SOTO VIERA, M.D.

**AUDIBILITE SPONTANEE DE LA VOIX MATERNELLE; AUDIBILITE CONDITIONNEE DE TOUTE AUTRE VOIX** (Audibilidad espontánea de la voz materna; audibilidad condicionada de cualquier otra voz), André-Thomas y S. Autgaerden, Presse Méd. 71: 37: 1761 (Sept., 1963), (Paris).

Desde los primerísimos días de la vida, el recién nacido responde a la voz de su madre, específica y electivamente, con movimientos de la cabeza o del cuerpo hacia el punto desde donde le llega ese estímulo sonoro. A menos de asociarse previamente con el llamado materno, cualquier otro sonido fracasa en provocar semejante respuesta.

¿Qué sabe el hombre del mecanismo tantas veces complicado de sus propios actos? André-Thomas pondrá este intrigante descubrimiento y traza analogías con los fenómenos del instinto que vemos en el reino animal, no sin preguntarse sobre el papel que pudieran desempeñar —en el comportamiento reputadamente subcortical de un sujeto como el recién nacido— los centros superiores. ¿No habrá, desde el período intrauterino, cierta iniciación o condicionamiento cortical del bebé a estímulos que provienen de la madre?

MANUEL E. SOTO VIERA, M.D.

**TREATMENT OF GAS GANGRENE WITH HYPERBARIC CHAMBER**, From The Children's Hospital Medical Center, 300 Longwood Avenue - Boston 15, Massachusetts.

A news release from The Children's Hospital Medical Center describes the case of a 17-year old girl who developed gas gangrene three days after an appendectomy and was failing to recover with penicillin, tetracycline and antitoxin. The infection has destroyed all the muscles of the right abdomen, was extending to the left, to the back and to the right thorax. She was placed in a hyperbaric chamber at three atmospheres, under anesthesia, with one hundred percent oxygen administered through an endotracheal tube; the oxygen saturation of her blood was increased from 100 - 120 mm. of mercury to between 1,000 and 1,800 mm. of mercury. The first session was for 2 hours, the second for 1-1/2 hours, and the remaining four sessions for an hour each.

The patient improved after the first three sessions. The Children's Hospital will accept any patients of all ages from anywhere for treatment of this condition since they have the only facility of this sort in operation in the United States.

J. E. SIFONTES, M.D.

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**PLASMA ERYTHROPOIETIN LEVELS IN CORD BLOOD AND IN BLOOD DURING THE FIRST WEEKS OF LIFE** ((Tasas plasmáticas de eritropoyetina en la sangre del cordón umbilical y en la del bebé durante las primeras semanas de vida), Halvorsen, S., Servicio de Pediatría y Laboratorio de Investigaciones Pediátricas, Rikshospitalet, Oslo (Noruega), Acta paediatrica 52: 5: 425 (Sept., 1963).

Las eritropoyetas, aparentemente, intervienen de igual modo en la eritropoyesis del recién nacido que en la de cualquier otro sujeto. Halvorsen estudió las tasas plasmáticas de eritropoyetina en bebés normales, en bebés eritroblastóticos y en bebés hipódicos; en todos altas, al nacer, caían progresivamente en los primeros mientras aumentaban en los demás. La carencia que fisiológicamente sobreviene en la eritropoyesis del recién nacido normal, se debe, con toda probabilidad, no a que falle en su función la médula ósea —pues en tal caso habría aumento de eritropoyetas, según sucede en las anemias por hipoplasia— sino a que mejorara la oxigenación de la sangre y con ello disminuye la necesidad de Hb.

MANUEL E. SOTO VIERA, M.D.

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**ESQUIZOFRENIA**, Leopold Bellak. Versión española del Dr. Ismael Antich 1128 páginas. Sobrecubierta de Rosa Martín. Editorial Herder, S.A., Barcelona, 1962.

Nada hay más apasionante en todo el vasto mundo de la psiquiatría y disciplinas conexas que el estudio de ese grupo, trágico y enigmático, de seres humanos que incluimos colectivamente para fines nosológicos en el llamado "Grupo de las Esquizofrenias". Mientras algunos sufren el trastorno en sus formas más violentas, en otros se manifiesta de modo benigno, como sucede en muchas de aquellas personas con quienes venimos en contacto en nuestro diario vivir y que nos chocan por lo "raras" que son. Aunque así no lo parezca, estas manifestaciones más benignas y menos dramáticas hacen sufrir más que la psicosis franca, ya que cuando ésta aparece, lo que indica es que el paciente se ha dado por vencido en su lucha y no le queda otro recurso que el de entregarse. Refúgiase entonces en un mundo fantástico de irrealidades y de sombras desde el que se le hace más y más difícil comunicarse con el resto de la humanidad, hasta hacérsele imposible: Se muere en vida.

Ante el dato irrecusable de que aquí en Puerto Rico, como en cualquiera otra parte del mundo civilizado, por lo menos *el uno por ciento* de la población adolece de este trastorno mental en alguna de sus protísticas formas, se hace indispensable un mejor conocimiento de lo que esquizofrenia significa y cómo se manifiesta. Todo médico, en cualquier especialidad a que se dedique, tendrá que ver esquizofrénicos a diario en su consulta, aunque no se entere de ello. Es por esto que le conviene aprender todo lo que pueda acerca de este interesante grupo de enfermos que, por diversas razones, venos con creciente frecuencia en nuestros tiempos.

La Editorial Herder de Barcelona nos ofrece ahora una excelente versión española del libro "Schizophrenia", interesante antología de trabajos origina-

les. Su autor principal es el Dr. Leopold Bellak, de Nueva York, internacionalmente reconocido como uno de los más asiduos y capaces investigadores y expositores de las esquizofrenias.

En el prólogo nos explica Bellak cómo no puede aplicársele un tratamiento uniforme al síndrome multiforme de "las esquizofrenias", ya que el síndrome no es debido a una causa única. Por otra parte se ha intentado, sin lograrlo, descubrir las causas específicas de este trastorno, y no ha habido posibilidad etiológica que no haya sido considerada alguna vez por neurólogos, geneticistas, biólogos, químicos, y por otros especialistas en diversos campos de la investigación científica. Bellak nos presenta con maestría su conocida "teoría unificada" que toma en cuenta múltiples factores quimiógenos, histógenos, genógenos y psicógenos; y elabora su concepto del síndrome esquizofrénico desde los puntos de vista fenomenológico y psicodinámico. Con estos criterios colócase el clínico en posición más sólida para poder establecer el diagnóstico diferencial, indispensable para aplicar la terapéutica adecuada.

El libro tiene dieciocho capítulos, todos ellos por reconocidas autoridades en diversos aspectos de las esquizofrenias. Entre los más interesantes podríamos citar, además de los del autor principal, los de Overholser y Werkman sobre etiología, patogenia y anatomía patológica, Herbert Weiner sobre diagnóstico y sintomatología, Harry Freeman sobre estudios fisiológicos, y el de Rudolph Ekstein y sus colaboradores en el estudio de la esquizofrenia y estados análogos en los niños. Los dos últimos capítulos, escritos por Paul K. Benedict nos hacen reflexionar sobre los factores socioculturales en las esquizofrenias y otros aspectos especiales de la cuestión, tales como la relación que pudiera haber entre esta enfermedad, la filosofía y el arte.

No debemos terminar esta reseña sin hacer mención de la ingente labor que representa la excelente traducción que ha hecho de la voluminosa antología el Dr. Ismael Antich. El libro, además, está impreso con esmero y nitidez, y es fácilmente manejable apesar de sus mil y pico de páginas. La bibliografía al final de la obra ocupa más de doscientas páginas y es una verdadera mina de referencias. Tanto el índice analítico como el índice de autores, ambos cuidadosamente preparados facilitan la búsqueda de información y acrecientan el gran valor que tiene este libro como obra de consulta sobre todo lo relacionado con su tema.

LUIS MANUEL MORALES, M.D.



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En toda reacción tisular inflamatoria, debida a traumas, fracturas, golpes, hematomas, etc., QUIMORAL acelera la reabsorción de sangre y linfa extravasadas, restablece la circulación local y abre paso a las defensas orgánicas. QUIMORAL domina la inflamación y el edema, alivia rápidamente el dolor y acelera la curación.

QUIMORAL, enzima antiinflamatoria para uso oral y absorción intestinal: en tabletas con actividad enzimática equivalente a 50.000 unidades Armour.  
Rp. Frascos de 16 y 32 tabletas.

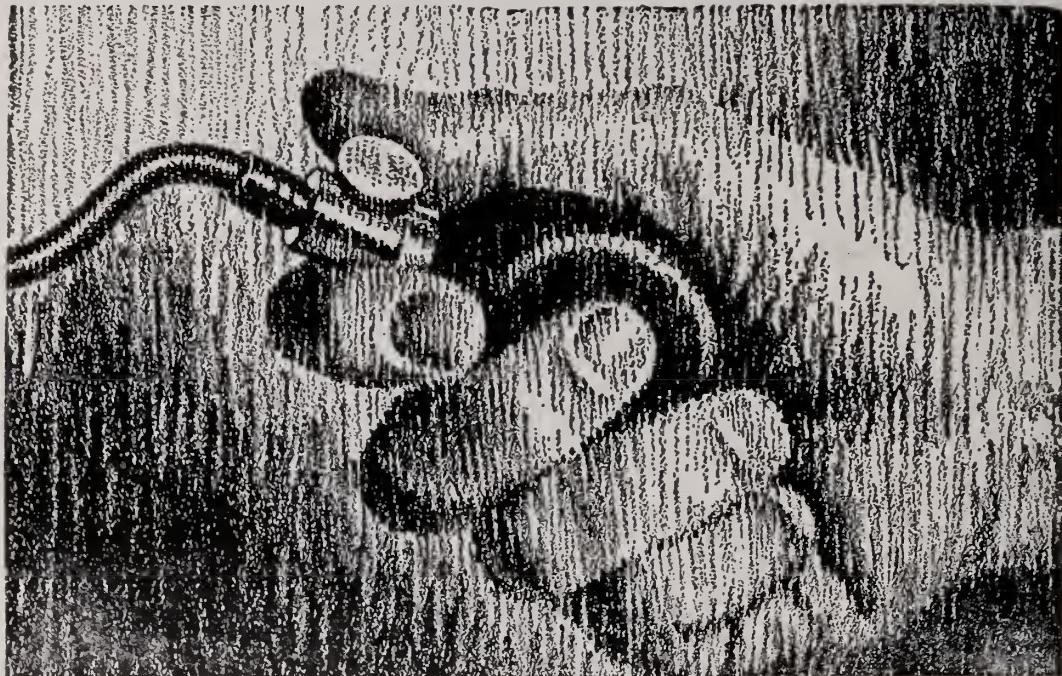
Nota.—Para indicaciones completas, contraindicaciones, posología, etc., consultar la literatura o la circular adjunta a los envases originales.



ARMOUR PHARMACEUTICAL COMPANY • Kankakee, Illinois, E.U.A.

hypertension

TABLETS  
**ALDOMET**  
TRADEMARK  
(METHYLDOPA)



**TO CONTROL HIGH BLOOD PRESSURE GENTLY, EFFECTIVELY, ACCEPTABLY**

Versatile in indications—recommended in sustained essential hypertension, and in those labile forms unresponsive to sedative therapy.

Effective "around-the-clock"—continuously and significantly reduces lying, sitting and standing pressure; simple dosage adjustment can prevent morning hypotension without sacrifice of afternoon control.

Conducive to normal, everyday activities—works while the patient works; exercise hypotension and diurnal blood pressure variations rarely occur.

Facilitates smooth management—ease of administration;

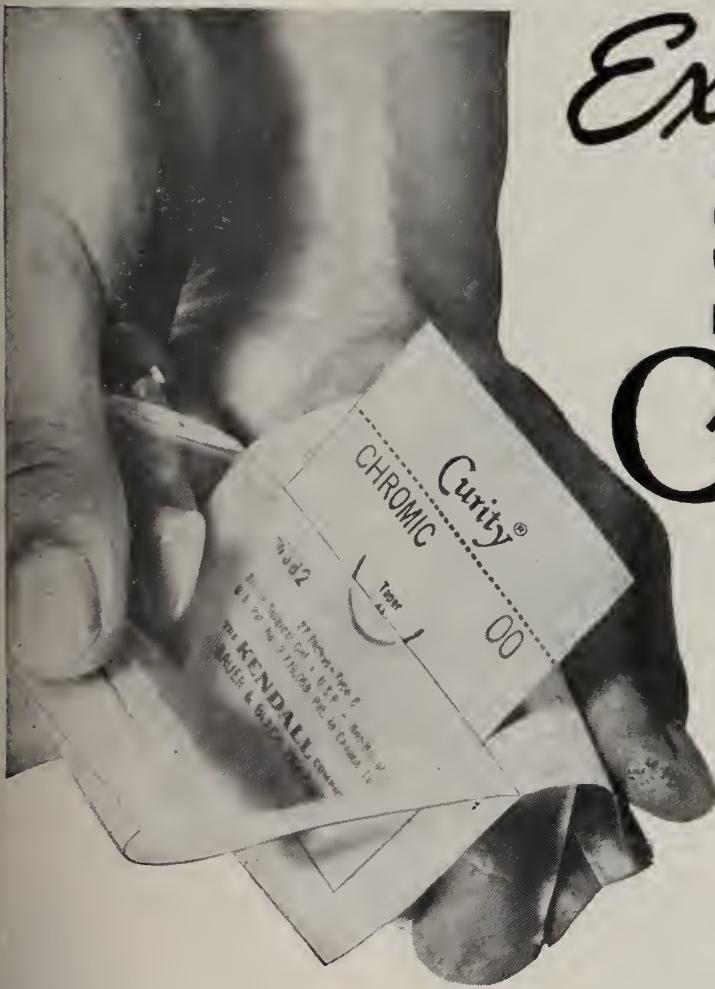
liberation from critical dosage titration; low incidence of side effects.

Oriented towards the ultimate goal of antihypertensive therapy—helps relieve the vital target organs from the strain of hypertension by effectively lowering blood pressure.

**Supplied:** Tablets ALDOMET (250 mg. methyldopa, each) in bottles of 30, 100 and 500.

**Note:** Detailed information on dosage, administration, Indications, precautions and bibliography is available on request.

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**1** Abrase el sobre exterior hasta la mitad, sujetándose de ambos lados.



**2** La enfermera toma el sobre interior con las manos con guantes esterilizados, o bien con una pinza estéril.



**3** Despréndase la parte superior del sobre...y se saca el carrete.

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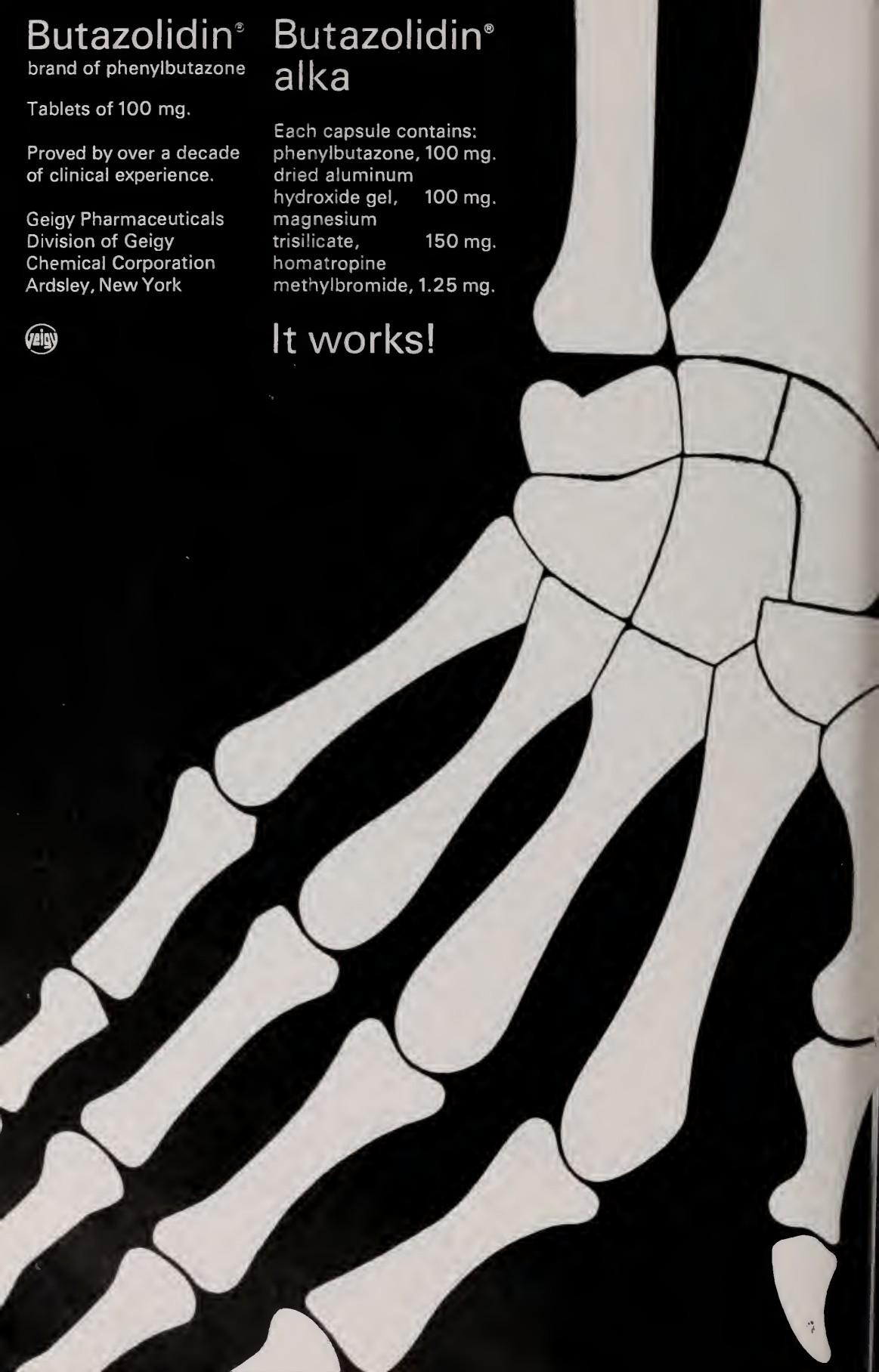
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# Butazolidin® alka

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phenylbutazone, 100 mg.  
dried aluminum  
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It works!

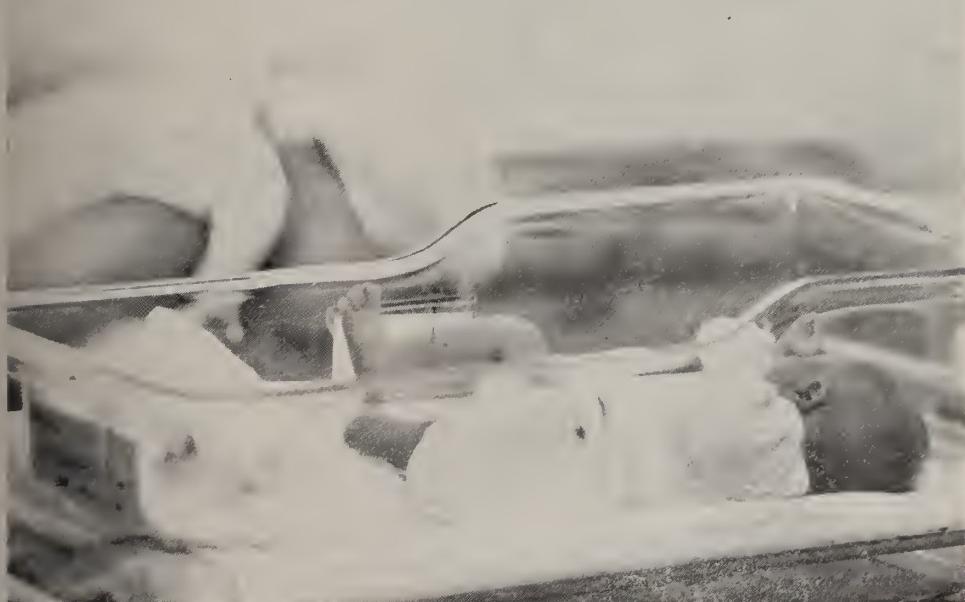


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Control with Dymelor as compared with other therapy in 1,140 patients.

*51.4% Improved with Dymelor*



Control with Dymelor in 172 patients considered to be "poor responders" to other oral agents.

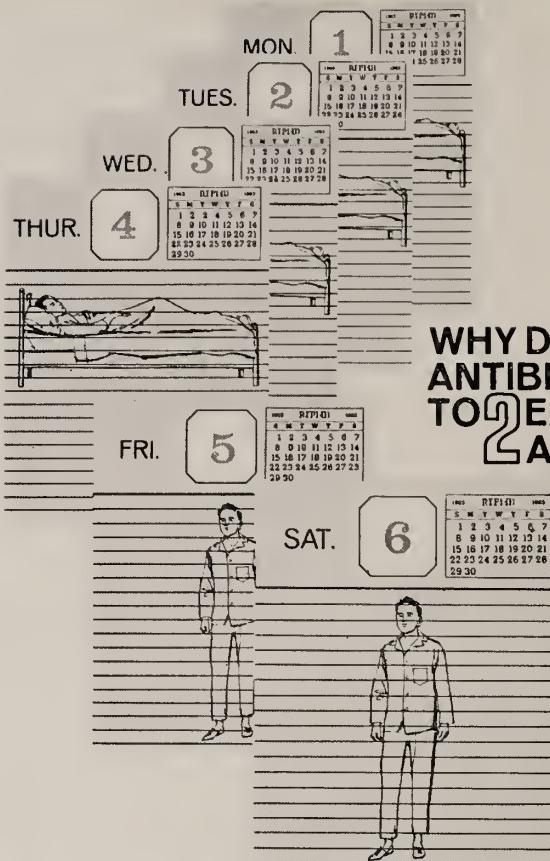
Number of Patients	Improved with Dymelor			Total Improved	
	Excellent	Good	Fair	Number	Percent
172	19	47	39	105	61

Note: 61 percent of poor responders to other oral agents improved when transferred to Dymelor.

450427

1. Accumulated Reports from 228 Clinical Investigators: Lilly Research Laboratories.





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ANTIBIOTIC GIVE UP  
TO 2 EXTRA DAYS'  
ACTIVITY?**

Because it is more resistant to disintegration, has a lower renal clearance rate than earlier tetracyclines'...a favorable depot effect resulting from protein binding and greater mg. potency...all giving higher, sustained *in vivo* activity which continues long after the last dose.

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# Boletín *de la* Asociación Médica de Puerto Rico

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ABRIL. 1964

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PUERTO RICO UNDER THE ACT OF AUGUST 24, 1912.

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Fundado en el 1903 y publicado mensualmente en San Juan, Puerto Rico

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El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudieran ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor se solicita de los autores que sigan las siguientes instrucciones:

a) Los trabajos deberán estar escritos a máquina a doble espacio y por un solo lado de cada página, en duplicado y con amplio margen.

b) En página separada debe incluirse lo siguiente: título (no excediendo de 80 letras y espacios), nombre del autor(es), grados académicos, institución y dirección postal del autor.

c) Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: (1) introducción, (2) material y métodos, (3) resultados, (4) discusión, (5) resumen (en español e inglés), (6) referencias.

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e) Las tablas, notas al pie y leyendas deben aparecer en hojas separadas.

f) Si un artículo ha sido leído en alguna reunión o conferencia debe así hacerse constar.

g) Deben usarse los nombres genéricos de los medicamentos. Pueden usarse también los nombres comerciales, entre paréntesis, si así se desea.

h) Se usará con preferencia el sistema métrico de pesos y medidas.

i) Las fotografías y microfotografías se someterán como copias en papel de histre sin montar. Los dibujos y gráficas deben prepararse a tinta negra y en papel blanco. Todas las ilustraciones deben estar numeradas (números árabigos) e indicar la parte superior de las mismas. Debe escribirse una leyenda para cada ilustración e indicarse en el texto donde debe ir colocada. Un máximo de 6 ilustraciones, por artículo, serán permitidas sin costo para el autor.

j) Las referencias deben ser numeradas sucesivamente de acuerdo con su aparición en el texto. Los siguientes ejemplos pueden servir de modelo:

6. Koppisch, E. Pathology of arteriosclerosis. Bol. Asoc. Med. P. Rico 46: 505, 1954. (artículo de revista)
4. Wintrobe, M. M. Clinical Hematology, 3rd Ed. Lea and Febiger, Philadelphia, 1952, p. 67. (libro)

Deben usarse solamente las abreviaturas incluidas en el Index Medicus, Biblioteca Nacional de Medicina.

Se podrán ordenar sobretiros del artículo cuando se reciba notificación de su aceptación.

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The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the understanding that it is to be published solely in this journal.

In order to facilitate review of the article by the Editorial Board and the preparation of the manuscripts for the printer the authors are requested to follow the following instructions:

a) The entire manuscript, including figure legends and references, should be typewritten double-spaced in duplicate with ample margins.

b) A separate title page should include the following: title (not to exceed 80 characters and spaces), author(s) name(s) and academic degrees, institution, and authors' mailing address.

c) Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: (1) introduction, (2) material and methods, (3) results, (4) discussion, (5) summary in English and Spanish, (6) references.

d) Case reports will include (1) introduction, (2) description of the case, (3) discussion, (4) summary in English and Spanish and (5) references.

e) Tables, footnotes and legends to figures should appear in separate sheets.

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g) Generic names of drugs should be used. Trade names may also be given in parenthesis if desired.

h) Metric units of measurements should be used preferentially. Abbreviations should be used sparingly.

i) Photographs and photomicrographs should be submitted as glossy prints, unmounted. Drawings and graphs should be made in black ink on white paper. All illustrations should be numbered (Arabic) and top indicated. A legend should be given for each and its location should be indicated in the text. A maximum of 6 illustrations is allowed without cost to the authors.

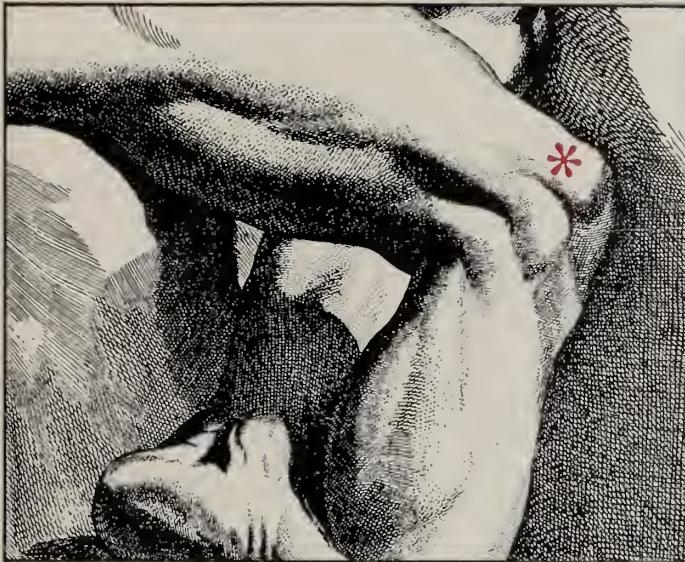
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to restore useful function in the  
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**CLINICAL CONSIDERATIONS. Indications:** Celestone (betamethasone, Schering) is indicated in the management of various allergic, dermatologic, ocular, rheumatic and other conditions known to be responsive to corticosteroid therapy.

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For complete product details, consult Schering literature available from your Schering representative, or Medical Services Department, Schering Corporation, Union, New Jersey.

**Packaging:** Bottles of 30, 100, 1000. Tablets of 0.6 mg. each. \*TRADEMARK CE-538-J-PR

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**new**

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relaxes muscle  
and relieves pain  
with virtually  
no side effects

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Diagnosis	Good	Fair	No Response	Total
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Muscle and Soft Tissue	117	42	6	165
Totals	182	77	14	273



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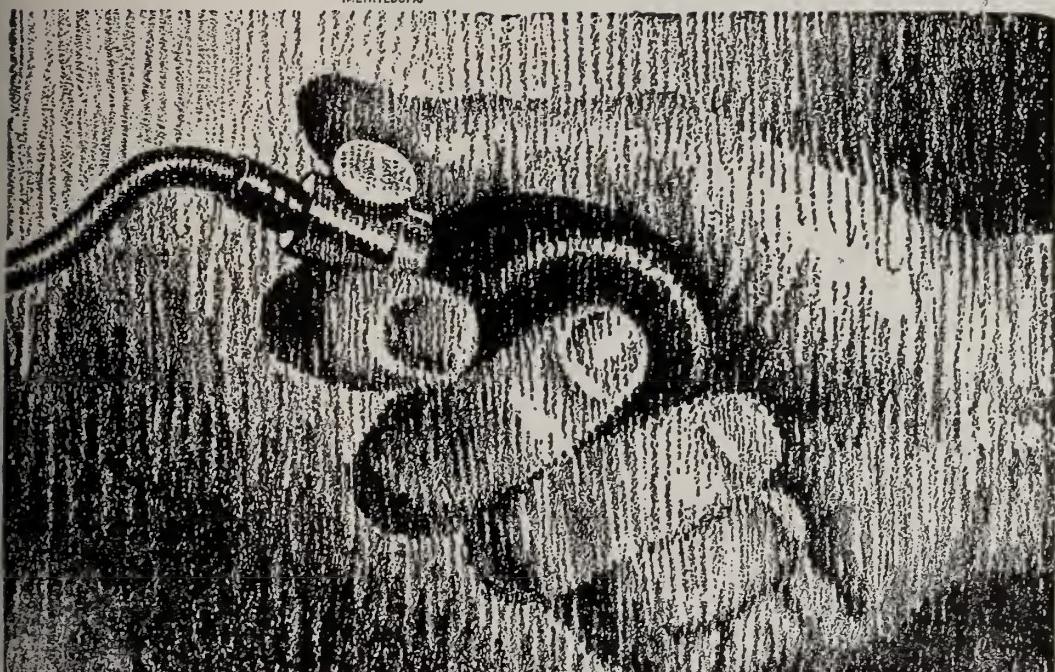
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# hypertension

TABLETS      TRADEMARK  
**Aldomet**  
METHYLDOPA



## TO CONTROL HIGH BLOOD PRESSURE GENTLY, EFFECTIVELY, ACCEPTABLY

Versatile in indications—recommended in sustained essential hypertension, and in those labile forms unresponsive to sedative therapy.

Effective "around-the-clock"—continuously and significantly reduces lying, sitting and standing pressure; simple dosage adjustment can prevent morning hypotension without sacrifice of afternoon control.

Conducive to normal, everyday activities—works while the patient works; exercise hypotension and diurnal blood pressure variations rarely occur.

Facilitates smooth management—ease of administration;

liberation from critical dosage titration; low incidence of side effects.

Oriented towards the ultimate goal of antihypertensive therapy—helps relieve the vital target organs from the strain of hypertension by effectively lowering blood pressure.

**Supplied:** Tablets ALDOMET (250 mg. methyldopa, each) in bottles of 30, 100 and 500.

**Note:** Detailed information on dosage, administration, indications, precautions and bibliography is available on request.

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Significantly  
lowers blood pressure...

yet does not depress  
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#### Now we'll show EUTONYL lower blood pressure!

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**ABBOTT LABORATORIES PUERTO RICO, INC.**

# antihypertensive



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PARGYLINE HYDROCHLORIDE

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#### **What is the usual effective dosage?**

In untreated adults under 65, the usual dosage is 25 to 50 mg. once daily. In clinical trials, control was usually achieved and maintained on a daily dosage of from 50 mg. to 75 mg. Adjustments should be made on response to therapy and blood pressure readings taken in the standing position. The dosage should not be adjusted more frequently than once every seven days. Tablets supplied in 10 mg.,

25 mg., and 50 mg. strengths.

**Can Eutonyl be used  
with other antihypertensives?**

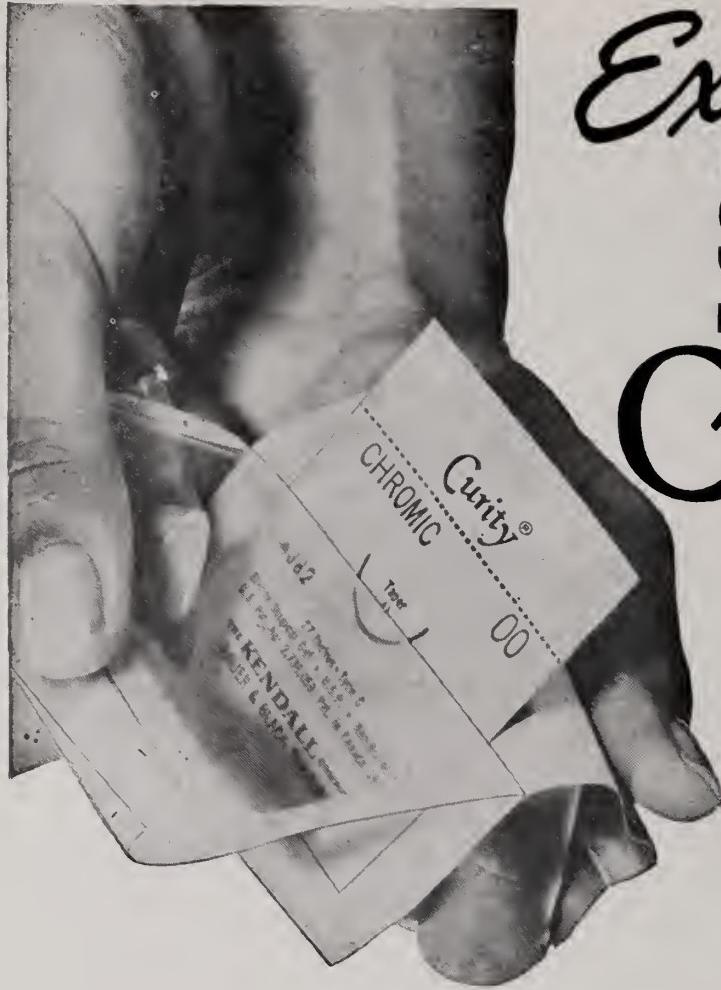
Yes. You may use Eutonyl alone or with other antihypertensive agents, including thiazides or thiazide-triawolfia combinations. Or as replacement for other nondiuretic antihypertensives. In such cases the starting dosage may be reduced.

See your Abbott Representative for full details and literature; or write to Abbott Laboratories Puerto Rico, Inc.

\*Significant—Minimum 20 mm. Hg. reduction in mean blood pressure† and/or achievement of normotension.

†Mean Blood Pressure—½ pulse pressure plus diastolic pressure.





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De fácil manejo y  
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**3** simples pasos para  
usar una sutura estéril en  
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sujetándose de ambos lados.



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con las manos con guantes esterilizados,  
o bien con una pinza estéril.



**3** Despréndase la parte superior del  
sobre...y se saca el carrete.



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International Division, Chicago 6, E. U. A.  
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*Exija*  
**SUTURAS Curity®**



Una nota de interés científico: Cuando surgen traumatismos o infecciones, la naturaleza establece una barrera de fibrina que los circunda. La ilustración que aquí aparece es una microfotografía electrónica de la fibrina ampliada a 46.000 diámetros. Esta notable obra original de C.V.Z. Hawn y K. R. Porter, se reproduce en este anuncio por cortesía de The Rockefeller Institute Press.

En traumatismos •  
reacciones tisulares  
postoperatorias •  
infecciones dérmicas

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reduce el período del tratamiento y su costo porque acelera la curación, a menudo un 50 por ciento.<sup>1</sup>

ANANASE es una enzima antiinflamatoria, oral, de origen vegetal.

Envase: Cajas de 12 y 48 grageas amarillas. Cada gragea contiene 50.000 unidades RORER de bromelina (enzima proteolítica)

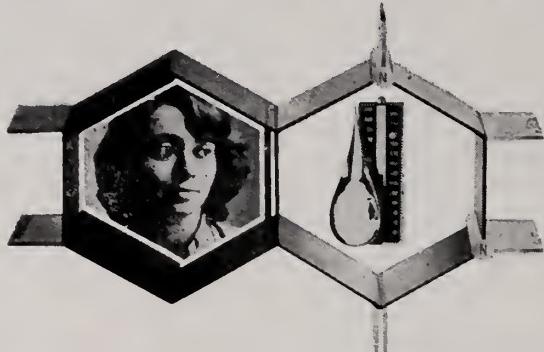
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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



WILLIAM H. RORER, INC., Fort Washington, Pa., EE. UU.

**G.B., 28, PREECLAMPTIC...**  
**ONE OF MANY WHO MAY GET**  
**A GOOD "START"...OR A GOOD "CHANGE"**



**Therapy:** One 50 mg. tablet daily for 30 days, plus bed rest and restricted activity.

**Results:** Weight down 12 pounds; blood pressure from 190/142 to 106/78. Completely satisfactory.

# Hydromox® moves fluid QUINETHAZONE

## NEW ANTIHYPERTENSIVE DIURETIC

Prompt, prolonged saluresis • sustained response on single morning dose • minimal nocturia • well tolerated with minimal K deficit • suited to combination therapy.

HYDROMOX quinethazone (7-Chloro-2-ethyl-1,2,3,4-tetrahydro-4-oxo-8-sulfamyl-quinalizine) is an antihypertensive diuretic which acts by inducing excretion of both sodium and chloride. Each tablet contains 50 mg. of quinethazone.

**Indications:** Edema caused by salt retention (as in congestive heart failure, nephrotic syndrome, hepatic cirrhosis, pregnancy, etc.), as well as some cases of lymphedema, idiopathic edema and edema due to venous obstruction; and hypertension, with or without edema.

**Dosage:** While 1 HYDROMOX quinethazone tablet (50 mg.) daily usually suffices, it may be necessary to raise

dosage up to 4 tablets daily (usually spaced) to elicit satisfactory response. When given with other antihypertensives, lower dosages of both agents may suffice.

**Side Effects:** Skin rash, GI disturbances, weakness or dizziness may occur, usually controllable by reducing dosage or correcting electrolyte imbalance. Pre-existing electrolyte abnormalities may be aggravated. Possibility of potassium depletion is greater in cirrhotics and digitalized patients. Foods rich in potassium may be desirable. Possibility of azotemia is greater in renal disease; and of hyperglycemia and glycosuria in diabetes. Photoallergy and hyperuricemia predisposing to gout have occurred. There may be a sudden drop in blood pressure when given with ganglionic blocking agents, veratrum or hydralazine, requiring reduction in dosage of these other drugs.

**Precautions:** Anuria.

\*From clinical data on file at Lederle Laboratories. Posed by model.

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CYANAMID BORINQUEN CORPORATION

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Santurce, P. R.

# BOLETIN

DE LA ASOCIACION MEDICA DE PUERTO RICO

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VOL. 56

ABRIL, 1964

NO. 4

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## HEREDITARY SPHEROCYTOSIS WITH LEG ULCER AND UNAFFECTED PARENTS OR SIBLINGS

### REPORT OF ONE CASE

Z. A. RIVERA BIASCOECHEA, M.D.\*

Toward the end of the nineteenth century, a familial form of jaundice was first recognized by physicians. It was later realized that it included several types of congenital hemolytic anemias, which depended on inherited abnormalities of the erythrocytes. Hereditary spherocytosis, hereditary elliptocytosis, hereditary non-spherocytic hemolytic anemia, Mediterranean anemia, sickle cell disease and other abnormal hemoglobinopathies have been described.

Wilson and Stanley,<sup>1</sup> and Minkowaki<sup>2</sup> were among the first to clearly describe most of the salient clinical features of the condition known today as Hereditary Spherocytosis, but also called at times spherocytic icterus, familial hemolytic anemia, and acholeluric jaundice. The disease is characterized by chronic anemia, increased hemolysis and erythropoiesis, jaundice, and splenomegaly. The classic feature of this hereditary condition is the presence, in the peripheral blood, of red cells that are spheroidal in shape and that are unusually susceptible to hemolysis when suspended in hypotonic media. Splenectomy in this disorder is usually effective in causing a cessation of the excessive red cell destruction, and relieving the anemia and jaundice. Nevertheless, the spheroidal red cell persists after the removal of the spleen.

It is the purpose of this report to present a case of Hereditary Spherocytosis in an 18 year old female, who was admitted to the hospital with an intractable ulcer on the leg, anemia, jaundice, and splenomegaly. The leg ulcer healed spontaneously, and the anemia and jaundice were relieved after splenectomy. The parents

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and siblings of the patient were investigated but no clinical or laboratory evidence of the disease was encountered.

#### CASE REPORT

An 18 year old female admitted to the Arecibo District Charity Hospital with the chief complaint of pain and an ulcer on the left ankle. Two years prior to admission, after trauma to the area, she developed the ulcer that has not healed in spite of therapy. On a previous admission to another hospital for the same condition, anemia and a palpable mass in the abdomen were found.

The past medical history revealed that since childhood she had been weak, pale and tired easily. At the age of 7 years, a low hemoglobin was found on a routine examination but no further studies were done. There was no history of abdominal pain or bleeding tendency. There were no other known cases of anemia in the family.

The physical examination on admission to the hospital revealed a pale, underdeveloped female for her age, with mild icterus of the sclera. There were no abnormal prominent features of the bones of the skull. The lungs were clear to percussion and auscultation. The heart was not enlarged to percussion and there were no palpable thrills. The rate was 90 per minute and regular, and the blood pressure was 130/90 mm. Hg. There was a soft, grade II, systolic murmur heard on the whole precordium with greatest intensity on the second left intercostal space. The liver edge was palpable one fingerbreath below the right costal margin, and the spleen was palpable four fingerbreaths below the left costal margin. There was an ulcer on the external surface of the left ankle of 2 cm. in diameter surrounded by indurated chronic granulomatous tissue. There was no edema or evidence of varicose veins. There were no spider telangiectasis, liver palms or other stigmatae of liver disease.

The laboratory studies revealed the following: hemoglobin 9.6 gm. per 100 cc.; R. B. C. 3.4 million per cu. mm.; platelet 187,000 per cu. mm.; W. B. C. 7,150 per cu. mm. with 52% segmented forms, 42% lymphocytes, 5% eosinophils and 1% monocytes; total blood protein 7 gm. per 100 cc. with 4.2 gm. albumin and 2.8 gm. globulin; total serum bilirubin 3.5 mg. per 100 cc. with direct bilirubin of 0.6 mg. per 100 cc. and indirect of 2.9 mg. per 100 cc.; Coomb's test (direct and indirect) negative; reticulocyte count 16%. The stool examination was negative for occult blood. Many spherocytes were seen in smears of the peripheral blood. Osmotic fragility of the red cells began at 0.48%, and was complete at 0.34%. Roentgenograms of the skull and chest were normal. The

bone marrow study showed erythroid hyperplasia. The urine was negative for bile but strongly positive for urobilinogen. The red cell survival time was 12 days (normal survival half time of cromated cells is 25 days or more). The splenic trapping was 4.39 (normal is no greater than 2). The sickle cell and L. E. cell preparations were reported negative. Osmotic fragility of red cells, after defibrinated blood was incubated for 24 hours under sterile conditions, began at 0.7% and was complete at 0.42%. The bleeding time, clotting time, serum glutamic oxalacetic and serum pyruvic transaminases were normal. The urinalysis and the Kahn serological test were negative. The reticulocyte count, and serum bilirubin determination were repeated several times with similar results as the above.

There was no improvement of the ulcer with local treatment to the area involved. Several blood transfusions were given and the hemoglobin was raised to 10.5 gm. per 100 cc.

The spleen was removed one month after admission to the hospital and the next day the hemoglobin was 12.6 gm. per 100 cc. and the R. B. C. was 4.5 million per cu. mm. Seven days after the operation, the reticulocyte count was 0.2%. Since then the hemoglobin continued above 12 gm. per 100 cc. and the R. B. C. above 4.5 million per cu. mm. The ulcer healed spontaneously and the icterus of the sclera disappeared. She was discharged from the hospital 10 days after the splenectomy.

The pathological study of the spleen was reported as follows: the organ weighed 450 gm. and the surface was of a dark gray color. On section, the splenic pulp was dark red and looked as if it were deeply congested with blood. Microscopically, the Malpighian bodies were small and widely dispersed, separated by pulp filled with blood. There was hyperplasia of the endothelial cells lining the sinusoids.

#### COMMENT

The family of the patient, including both parents and eight siblings, was investigated (table 1). Physical examination, hemoglobin determination, reticulocyte count, study of peripheral blood, osmotic fragility of the red cells, and osmotic fragility after 24 hours incubation of defibrinated blood were done.

The physical examination failed to reveal jaundice or splenomegaly in any member of the family. As shown on table 1 the laboratory studies were normal. Neither spherocytes or unusual susceptibility of the erythrocytes to hemolize, when suspended in hypotonic media, were evident in any member of the family.

TABLE I  
SURVEY OF THE FAMILY OF A CASE OF HEREDITARY SPHEROCYTOSIS

Members of the family	Age	Hemoglobin in gm. per 100cc	Reticulocyte count	Spherocytes in smear of peri- pheral blood		Osmotic fragility of erythrocytes		Osmotic fragility of erythrocyte after incubation			
				Beginning	Complete	Beginning	Complete	Beginning	Complete		
Patient after surg.	18	12.7 gm.	0.9%	Many		0.48%		0.32%		0.7 %	0.38%
Father	60	13.7 gm.	0.5%	None		0.46%		0.26%		0.5 %	0.32%
Mother	56	12.7 gm.	0.3%	None		0.44%		0.28%		0.5 %	0.34%
Sisters											
A	26	12 gm.	1.1%	None		0.44%		0.30%		0.5 %	0.24%
B	21	13 gm.	0.3%	None		0.42%		0.28%		0.48%	0.24%
C	23	13.4 gm.	0.5%	None		0.44%		0.28%		0.5 %	
D	14	14.1 gm.	0.4%	None		0.44%		0.26%		0.5 %	0.30%
Brothers											
A	21			None		0.40%		0.30%		0.5 %	0.36%
B	20	12.3 gm.	0.1%	None		0.44%		0.26%		0.48%	0.14%
C	16	13 gm.	0.5%	None		0.42%		0.26%		0.5 %	0.32%
D	13	12.7 gm.	0.7%	None		0.44%		0.26%		0.5 %	0.34%
Control	38	14.5 gm.	0.5%	None		0.44%		0.26%		0.5 %	0.36%

## DISCUSSION

The studies of Race<sup>3</sup>, Meulengracht<sup>4</sup> and others indicate that hereditary spherocytosis is probably inherited as a Mendelian dominant. In the families studied by Race<sup>3</sup> and by Young<sup>5</sup> there was a shortage in the expected number of affected siblings (24% instead of the expected 50% incidence). The factors attributed for this are the following: 1.) an unusually high miscarriage rate and infant mortality of affected compared with unaffected siblings, and 2.) variation in penetrance leading to mild and easily missed forms of the disease.

In four out of the 26 families studied by Race, in 5 out of 28 families studied by Young, and in one family reported by Meulengracht both parents of an affected propositus were apparently unaffected. But some siblings in several of those families on which the parents were apparently unaffected, revealed hematologic abnormalities like those of hereditary spherocytosis.

The parents or siblings of the patient presented in this report, revealed no evidence of abnormal erythrocytes. Several possibilities have been proposed to explain the absence of hematological abnormalities in the parents of patients with hereditary spherocytosis. The possibility that one of the parents carries the gene for HS but that the gene penetrance or expressivity is such as to be undetectable by available methods (carrier state) has been proposed by Dacie.<sup>6</sup> Other possibilities are gene mutation on the propositus, illegitimacy (considered very unlikely in the reported patient) and occurrence of an HS like disease that is either non-hereditary or at least not inherited as a Mendelian dominant. The latter, is a very likely possibility in the case presented.

The patient also revealed other uncommon feature of the disease. Intractable leg ulcers not associated with varicose veins, are a remarkable but rather uncommon complication of hereditary spherocytosis. In the series of cases reported by Young no ulcer of the legs was noted. Ulcer of the legs in young patients with HS has been reported by Dedichen<sup>7</sup> and by Taylor.<sup>8</sup> The pathogenesis of such ulcers is obscure since there is no reason to postulate vascular occlusion by the red cells in this disease, as there is in sickle cell anemia.

As a rule the ulcer heals quickly after splenectomy. In the case reported she had an intractable leg ulcer for over two years with no improvement in spite of continuous therapy. There was marked improvement only after the spleen was removed, and it was almost completely healed two weeks after the operation. There has been no recurrence of the ulcer since then.

## SUMMARY

A case of hereditary spherocytosis with an intractable leg ulcer and absence of family history of the condition has been presented. The patient evidenced marked clinical improvement, including healing of the ulcer after splenectomy.

A survey of the family including physical examination, hemoglobin determination, reticulocyte count, study of the peripheral blood and osmotic fragility of the red cells failed to reveal any of the classical features of the disease. The possibility of an acquired form of the disease or at least not inherited as a Mendelian dominant has been proposed.

## RESUMEN

Se presenta el caso de una paciente que sufre de esferocitosis hereditaria con úlcera en la pierna izquierda resistente a tratamiento; y ausencia de la enfermedad en la familia.

Se incluye estudio practicado en la familia el cual no revela evidencia de la enfermedad en ninguno de los miembros. Este estudio sugiere la posibilidad de que exista una forma adquirida de esta enfermedad.

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## BLOOD-ALCOHOL LEVELS AND THE DRIVER\*

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The constant increase of Death on our highways as a result of motor vehicles accidents should be of great concern to us all. These accidents are a result of many factors. Of these many factors, alcohol and man play no little role.

The following information is therefore presented with the hope that it may be useful when questions arise pertaining to the relationship between blood-alcohol values and the condition referred to as "being under the influence", especially as related to ability to operate motor vehicles safely.

### 1. Actions:

Ethyl alcohol is a central nervous system depressant, acting in a manner similar to that of the general anesthetics such as ether and chloroform. It also acts as a social lubricant. Shyness and inhibitions are diminished. Conscience, conformity and social restraints are blunted, and "one's true inner self" may now be revealed.<sup>1,2,3</sup>

### 2. Absorption:

Alcohol requires no digestion, and absorption occurs apparently by simple diffusion from the stomach and intestines into the blood stream. This diffusion is so rapid that from 80-90% of the ingested quantity may be absorbed in about 30 minutes, although complete absorption may require approximately 2 hours. About 20% is absorbed from the stomach and the remainder from the small intestine. A delay in gastric emptying time is a most important factor in slowing the rate of absorption. Largely because of this, the speed of absorption may vary between individuals and in the same individual at different times. Ordinarily the most important factor in delaying absorption is the presence of food (any food); carbohydrates and proteins being equally or possibly more effective than fats in this respect. The concentration and nature of the alcoholic beverage are also influencing factors; for instance, the alcohol in beer is more slowly absorbed than that in an equal concentration in water. A "highball" type of drink diluted is rapidly absorbed and the soda water ( $\text{CO}_2$ ) even hastens this.

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The more concentrated "on the rocks" drinks are more slowly absorbed.<sup>1,2,3</sup>

### 3. Fate:

Approximately 95% of the alcohol absorbed is completely metabolized to CO<sub>2</sub> and water. The initial stage of this metabolism begins in the liver, hence the possible effect of liver disease on the intensity of the alcohol activity. The remaining 5% is eliminated unchanged chiefly by the lungs and kidneys. Normally the body destroys and eliminates alcohol at a rate equivalent to about 3/4 oz of whisky (100 proof) per hour. In terms of changes in the blood-alcohol percentage, this corresponds to a decrease of approximately 0.02% per hour.<sup>4</sup>

### 4. Individual Tolerance:

This depends upon congenital or acquired tissue (brain) susceptibility, rate of absorption, rate of elimination, age and the general medical and physical condition of the subject. Individuals tired, or in bad health organically, mentally or physically, are usually more profoundly affected by alcohol than those in a state of good health.

### 5. Usual Methods of Testing:

Direct determination of the concentration of alcohol in the blood by chemical or physical analysis is the most reliable and practical method. Indirectly, blood-alcohol levels may also be determined by analysis of the expired air for alcohol. The validity of these tests, of course, depend upon the Special training of the chemist.

### 6. Synergisms:

Subjects taking any depressant drugs such as the barbiturates, morphine derivatives, chloral hydrate etc. concomitantly with alcohol will be more markedly affected than otherwise. Such drugs should be used only with special care in the presence of alcohol, if at all. Death due to this synergistic action is not uncommon.<sup>4</sup>

As a matter of fact, any depressant drug in itself, also will adversely affect the driving ability. One should NOT DRIVE if he has taken a depressant drug.

### 7. Action (Signs and Symptoms):

These are fairly typical and are generally characterized by a release from the usual restraints. As a result there is the appearance, initially at least, of stimulation; actually this is a pseudo-stimulation. Depending on the amount taken, there is a sense of security, a feeling of being a "superman", a "nothing-matters-plenty-of-time" attitude, hilarity and boisterousness.

Especially affected and blunted are judgment, mental concentration, alertness, sharpness of vision, reflex action and motor co-ordination. There is also present some mental confusion, impulsive behavior, clumsiness, slow and sluggish thinking, analgesia and decreased efficiency in responding to emergency situations and inability to perform simple tasks with normal speed and accuracy.

Other findings are nausea, vomiting, vertigo, warm inner glow, sweating, slurred speech, flushed face, dilated pupils, unsteady gait, loquaciousness, sleepiness, diuresis, rapid pulse, dyspnea, cerebral edema, respiratory depression, cyanosis, coma, circulatory collapse and even death (\*depending upon severity).<sup>5</sup>

### 8. Interpretation of Blood-Alcohol Values: (Largely from the National Safety Council)

Less than 0.05% - *prima facie* evidence that the subject is not under the influence of alcohol.

0.05% - 0.10% - corroborative evidence to be considered with outward physical symptoms. In general, the nearer the level of 0.10% is approached, the more likely the subject is of being under the influence of alcohol.

0.10% and above - *prima facie* evidence that the subject is under the influence of alcohol insofar as the operation of a motor vehicle is concerned.

0.25% and above - the subject is markedly intoxicated.

0.40% and above - comatose levels of alcohol which may lead to death.<sup>7</sup>

### 9. Approximation of Alcoholic Beverages to Reach a Given Blood-Level:

A 12 oz. bottle of beer (4%) contains approximately the same alcohol content as 1 oz. of whisky (100 proof). For an average 160 pound individual tested within 30-45 minutes after drinking; a minimum of:

\* Death is not uncommon. Acute alcoholism kills more adults annually than any other single poison.<sup>6</sup>

2 oz. whisky - 0.05% alcohol in blood

4 oz. whisky - 0.10% alcohol in blood

6 oz. whisky - 0.15% in blood

8 oz. (1/2 pint) - 0.20% alcohol in blood

Other things being equal the greater the body weight the larger (in rough proportion) must be the alcohol intake to achieve an equal alcohol value.

#### DISCUSSION

The use of alcoholic beverages has been commonplace for many centuries and dates back even to the beginning of history. It is no wonder that at least 60,000,000 Americans drink; it is pleasant to the taste and furthermore provokes the individual with a feeling of "Well being". It is with reason that Osler called it the "milk of old age" and others the "liquid of life". It lessens the bitterness of memories and low spirits, and can summons sleep. It stimulates appetite, is good as a tranquilizer and may even lengthen life if handled prudently; providing one is not killed in the meanwhile in a motor vehicle accident. It is indeed a sad situation when more people were killed on our American highways than were killed during the Korean War; and that in at least 30 per cent of these fatalities, alcohol was a factor. **The "Drinking Driver" must in some way be Curbed!** This will not be easy. The offenders are unique, in that normally they are law-abiding citizens and in some cases even of some social status. Therefore, an enterprising defense is always trying to discredit the scientific evidence in the eyes of the court.

#### SUMMARY

In spite of past and present efforts, by the National Safety Council and Law Enforcement Agencies, The Drinking Driver is on the increase. Drinking to any extent reduces the ability of any driver. For this reason, the social drinker is a greater menace than is generally known. His judgment is impaired with fairly low alcohol levels and he by far out numbers the obviously intoxicated drivers.

Judgment impairment occurs before more obvious symptoms of intoxication. One does not have to be obviously intoxicated to be an unsafe driver. **"Under The Influence"** means that due to drinking alcohol, a person has lost to any degree some of his normal faculties of judgment and his ability to respond to an emergency situation as he would otherwise if he had not been drinking.

## SUMARIO

A pesar de los considerables esfuerzos hechos por el Consejo General de Seguridad y las distintas agencias para el cumplimiento de la ley, el conductor que guía bajo los efectos de las bebidas alcohólicas desafortunadamente ha ido en aumento. Toda bebida alcohólica ingerida, no importa su cantidad, tiende siempre a disminuir la habilidad de cualquier conductor de vehículo de motor. Por esta razón, el individuo que acostumbra sólo a beber en forma social (lo que se llama en inglés "social drinker") constituye una mayor amenaza social de lo que es generalmente estimado en cuanto a conducir un auto se refiere. Su juicio aún bajo los efectos de pequeñas cantidades de alcohol es deficiente, por lo que resulta mucho más peligroso - debido a su mayor número - que el conductor que obviamente está completamente intoxicado y que por lo general son los menos en calles y carreteras.

Deficiencias en el juicio ocurren mucho antes de que los síntomas de intoxicación se hagan evidentes. No es necesario estar obviamente intoxicado para ser un conductor negligente e inseguro.

Estar **bajo los efectos del alcohol**, significa, que la persona debido a la ingestión de bebidas alcohólicas ha perdido en un grado variable sus facultades normales de juicio y su habilidad normal para responder a situaciones de emergencia que en otra forma la tendría si no hubiera estado ingiriendo bebidas alcohólicas.

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## INTUSSUSCEPTION IN ADULTS

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### Introduction:

Intussusception is a disease of childhood and infancy primarily and, after the first month of life, it is second to appendicitis as a cause of acute abdominal emergencies. Although uncommon, it is not rare in adults, accounting for about 3% to 10% of all cases of intussusception.

The literature on adult intussusception is sparse, only 1267 cases having been reported up to 1961. Three additional personal cases constitute the basis of this report and are being added to the medical literature.

### CASE REPORTS

Case Report #1: M. R. R. is a 53 year old colored male, admitted to the hospital on October 12, 1957, with a ten day history of vague abdominal pain, generalized myalgias, and increasing constipation. There was no blood in the stool, nausea or emesis. The patient was placed under observation, a mass was felt in the right lower quadrant, and the possibility of walled perforated appendicitis with possible carcinoma of the cecum was considered. However, while under observation and while preparing him for diagnostic X-rays, the pain increased in severity and the mass migrated, and two days later, it was possible to feel it in the right upper quadrant of the abdomen at the time of aggravation of the pain. The diagnosis of intussusception was then considered and an emergency abdominal operation was undertaken on October 14, 1957. At operation, an ileocolic intussusception was found with the head of the intussusceptum in the hepatic flexure of the colon. A right hemicolectomy and terminal ileumectomy with ileotransverse colostomy was performed without the aid of bowel preparation. The pathological findings was of a benign ulcer of the cecum with ileocolic intussusception. The postoperative course was uneventful.

Case Report #2: B.M.F. is a 21 year old white female, who was admitted to the hospital on October 18, 1957. She complained of generalized abdominal pain of two days duration, accompanied by nausea and emesis. She had had constipation of four days duration. Melena had occurred four months prior to this illness. The pertinent findings on physical examination were limited to the lips, oral mucosa, and abdomen. She was gravid with the

uterus palpable at the umbilicus, and a sausage shaped mass, somewhat movable, was felt just above and to the left of the umbilicus. There was no blood in the stool. The lips and oral mucosa presented brown, discrete areas of pigmentation, as seen in cases of Peutz-Jeghers syndrome. A presumptive preoperative diagnosis of intussusception due to small bowel polyps was made, and at operation, six hours after admission and two hours after surgical consultation, an intussusception of the upper jejunum was found, resected en bloc, and found to have a gangrenous segment of jejunum with two polyps. A jejuno-jejunostomy, end-end type, reconstituted the continuity of the intestine. She developed a mild thrombophlebitis of the right leg, which responded to conservative measures. The patient was discharged thirteen days after admission in satisfactory condition.

**Case Report #3:** J. M. M. is a 38 year old white male, admitted on October 8, 1961, because of abdominal pain of five days duration. He had had emesis for the past five days and a partial gastrectomy with gastroduodenostomy had been done on September 5, 1961, for an antral gastric benign ulcer. On admission, the abdomen was slightly distended and a flat plate of the abdomen revealed some distention of the upper jejunum. Hydration and partial correction of electrolytic imbalance were carried out in the next 24 hours and, on October 9, 1961, an exploratory laparatomy was performed following a preoperative diagnosis of an obstructing adhesion. An intussusception of the upper jejunum was found, resection of the affected segment of the bowel was performed, and continuity was re-established with end-end anastomosis. Pathological examination revealed hemorrhagic infarction, with small granulomas of unspecified etiology, of a segment of intussuscepted jejunum. The postoperative course was uneventful, in spite of a superficial wound infection.

#### DISCUSSION

In children, the disease is usually acute with typical colicky pain and apparent well being between pains. It occurs in males in about 60% of the cases and there is an organic cause in only 5% of the cases to explain the intussusception. The other 95% of the cases remain unexplained or idiopathic. In adults, the picture is usually atypical, of longer duration as a rule, and with varied symptoms. Gross blood in the stools is a late symptom, usually indicative of hemorrhagic infarction in the intussusceptum. A palpable mass is found at times, especially if there is no distention. This mass may shift in position, as from the right lower to the right upper quadrant of the abdomen. In 80% of the cases there

is an organic cause and in about one third it turns out to be a carcinoma of the colon. In children, the 5% caused by an organic lesion is made up of Meckel's diverticulum, benign polyps, and reduplication, in that order of frequency. As people live longer, an increase in organic lesions of the colon would naturally occur and an increase in adult intussusception could be expected.

As in most cases of infant intussusception, the treatment of adult intussusception is surgical. In selected cases of ileocolic intussusception in infants, hydrostatic reduction may be tried, but it should not be considered in adults. In fact, at the time of operation, the surgeon should be extremely careful not to attempt reduction in the adult cases because of the high incidence of organic lesions and the great likelihood of carcinoma, with the danger of spreading tumor cells into the portal circulation or seeding tumor cells into the peritoneal cavity. In adults, resection without reduction should be performed, if possible. This, of course, is not necessary in infants, unless there is gangrene of the intussusceptum.

#### SUMMARY

Personal experience with three cases of adult intussusception confirms the general impression that, more often than not, it is a disease of a chronic nature with atypical pictures. It differs in various ways from its counterpart in children, and this should be considered in handling these cases. In handling adult cases, the surgeon should be aggressive and be prepared to perform a cancer operation, since a large number of these patients turn out to have carcinoma. Reduction in these cases is to be condemned.

#### RESUMEN

Experiencia personal con tres casos de intususcepción en adultos confirme la impresión general de una enfermedad con tendencia a cierta cronicidad y cuadros atípicos en muchas ocasiones. Tiene varios puntos que la hacen una enfermedad distinta a la presentada por los niños. Al manejar estos casos, el cirujano debe ser agresivo y estar preparado para hacer una resección de cáncer, ya que un buen número de estos pacientes tienen un carcinoma como causa incitante de la intususcepción. La reducción de intestino con intususcepción en adultos debe ser condenado, pues no es racional ni beneficiosa para el paciente.

## THE POSTANESTHETIC ELECTROCARDIOGRAM\*

DR. RAMON M. SUAREZ, SR.; DR. ALBERTO LUGO and  
DR. RAMON M. SUAREZ, JR.\*\*

Studies on the postanesthetic electrocardiogram are relatively scarce, as far as we have been able to ascertain, and we thought that their possibilities, if any, had not been adequately explored in Puerto Rico.

Electrocardiograms before and shortly after operation were taken on one hundred consecutive surgical cases admitted to Hospital Mimiya. All were white patients; sixty males and forty females. The youngest patient was 4 years old, the oldest 87. Grouped by age there were 7 patients between 4 and 20 years; 22 between 21 and 40; 30 between 41 and 60 and 41 between 60 and 87 years. In this last group there were 7 octogenarians.

The operations performed varied from simple cystoscopy to subtotal gastrectomy. Prostatectomy was the most frequent operation performed. Twenty two patients underwent either transurethral or suprapubic prostatectomy. Cataract operation was second. It was performed on 10 patients. Exploratory laparotomy on 6, biopsy of the breast on 5, thyroidectomy on 5, and hemorroidectomy also on 5. There were 4 tonsillectomies, 4 herniotomies, 3 cholecystectomies, 2 colectomies, 2 nephrectomies, 2 sympathectomies, 2 reductions of fractures, one of them with nailing, 2 cystostomies, and then a miscellaneous group of operations which included among others, tumor of the bladder, vesicovaginal fistula, Meckel's diverticulum, glaucoma, strabismus, cystocele and rectocele, pilonidal cyst, laminectomy, Marshall Marchetti's operation, and implantation of radon.

### Anesthesia

Patients were personally visited and evaluated for anesthesia the evening before surgery with the special aim of establishing rapport by answering questions and doubts and inspiring the necessary confidence so as to promote a relaxed attitude.

Premedication consisted usually of a barbiturate (Nembutal gr. 1-1/2) one and a half to two hours before surgery, followed by scopolamine or atropine grs. 1/150 with Demerol 25 to 100 mg. intravenously 45 minutes to one hour before the operation. This was complemented in some apprehensive patients with meprobamate 400 mg. or Vesprin 25 mg.

General anesthesia consisted mainly of Pentothal intravenously in doses from 200 to 300 mg. for induction followed by nitrous

\* Read at the annual meeting of the Asociación Médica de P. R., Nov. 14, 1963.

\*\* From Fundación de Investigaciones Clínicas, Santurce, Puerto Rico.

oxide and oxygen, 1-1/2 to 3 liters, administered by mask or via an endotracheal tube and Succinyl Glucose intravenously as muscle relaxant. Demerol intravenously in divided doses was frequently used for analgesia. Respirations were controlled or assisted. Ether and oxygen was used in a few cases with spontaneous respirations allowed.

Spinal anesthesia was employed using Pontocaine made hyperbaric with equal amounts of 10% glucose in water. This was complemented with 0.2cc. of adrenaline chloride in 1:1000 solution to prolong anesthesia only in a few cases where extremely long duration was anticipated. The level of the anesthesia was achieved mainly by varying the degree of Trendelenburg's position according to the requisites of the proposed surgical intervention. It may be interesting to note that Pentothal intravenously in dose of 150 to 250 mg. was given just prior to the insertion of the needle in most cases. No local anesthetic was used to introduce the spinal needle. This short sleeping dose of Sodium Pentothal, by eliminating all psychic reactions has been a very technique in the patient's experience, and facilitated the accurate and rapid introduction of the spinal needle.

A number 26 gauge needle was employed to puncture the dura. This eliminated the post spinal headaches. In some cases Nembutal intravenously in doses of 50 to 100 mg. was administered for sedation during spinal anesthesia as a basal sleeping dose. On a few cases Vesprin, 8 to 15 mg. intravenously was employed to control restlessness and/or nausea. When nausea alone occurred without hypotension during spinal anesthesia Tigan or Torrecan 100 to 200 mg. was administered intravenously with immediate excellent results. The frequent tendency to hypotension during spinal anesthesia was controlled by a slow drip of Neosynephrine, 10 mg. in 500 cc. of 5% glucose in water.

We do not routinely administer oxygen to patients under spinal anesthesia. Oxygen by mask 100% may be temporarily given while an acute period of hypotension is being controlled by blood or vasopressor drugs, or if the level of the spinal anesthesia happens to be higher than the upper thoracic dermatomes.

Sodium Pentothal was used as the sole anesthetic agent in 2.5% solution in 5 cases. The dose varied from 200 to 600 mg. Oxygen by mask was occasionally used to insure adequate oxygenation. Nitrous oxide and oxygen supplementation was resorted to in a few cases to keep the total dose of Pentothal low whenever surgery was prolonged.

Topical Pontocaine 1/2% and retrobulbar 2cc. of 2% Novocaine with a minimal dose of adrenaline was used in 3 cases. The usual premedication had been previously given. Local anesthesia

was used in another 2 cases. Spinal anesthesia in 19 cases, spinal and general anesthesia in 7 cases, and general anesthesia in 64 cases.

### The Electrocardiogram

The classical 12 leads were taken on all patients. A well calibrated direct writing apparatus was used. The three standard leads and the unipolar limb leads were taken with normal sensitivity, 1 cm. = 1 millivolt. The unipolar precordial leads with half-normal sensitivity, 2 cm. = 1 millivolt.

The heart rate increased slightly or moderately after operation in 59 patients, it remained the same in only 4, but its frequency decreased in 37 patients.

The QRS complexes showed originally no axis deviation in 45 of the 100 subjects, 54 showed left axis shift, and right axis shift was observed in only one instance. No change in axis was observed in most of the cases following operation. Only 2 cases which originally showed no axis shift turned to left axis following operation, 1 turned right, and another case which showed left axis deviation originally became normal after operation.

The P-R interval varied from 0.12 to 0.24 seconds before operation. No significant changes were observed in the post-operative period, except minimal variations which were probably consistent with changes observed in heart rate.

The S-T segments were found isoelectric in all but 7 patients before operation. Of these, 6 were slightly depressed and 1 slightly elevated. No changes were observed postoperatively except in 1 case (No. 9) who showed sagging before operation and slight elevation of ST segments in leads 2 and 3 following the surgical intervention. This patient was a 73 years old man in whom a cystoscopy was performed under general anesthesia. His heart rate was 82 preoperatively and 64 postoperatively.

The QT ratio varied between 0.80 to 1.25. It remained unaltered following operation in 12 patients. It increased in 50 and it decreased in 38.

The QTc ratio ranged between 0.31 to 0.51 preoperatively. Following the operation the QTc ratio remained the same in 8 patients, it increased in 51 and was less than originally in 41 patients.

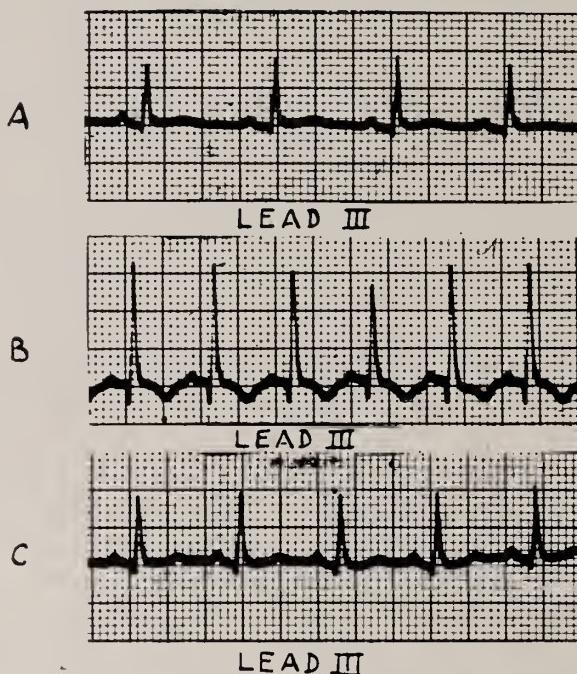
Alterations in the T waves of the electrocardiogram were the changes most frequently observed. Upright or isoelectric T waves

before operation, became negative after operation in 12 cases, but the changes were neither marked nor persistent. Changes in the T waves were limited to lead aVL in 6 of the 12 cases. In one of them (Case 23) the negative postanesthetic T wave in aVL was accompanied by a small Q wave. These changes reverted to normal three days later.

On the other hand in Case 25 we found that negative T<sub>1</sub>, T<sub>2</sub> and negative T waves in V<sub>4</sub>, V<sub>5</sub> and V<sub>6</sub> found before operation, changed to upright T<sub>1</sub> and T<sub>2</sub> and T in V<sub>4</sub> postoperatively. Postoperatively negative T waves were limited to V<sub>5</sub> and V<sub>6</sub>. A negative T in a VL before operation became isoelectric postoperatively in Case 18.

#### Illustrative Cases:

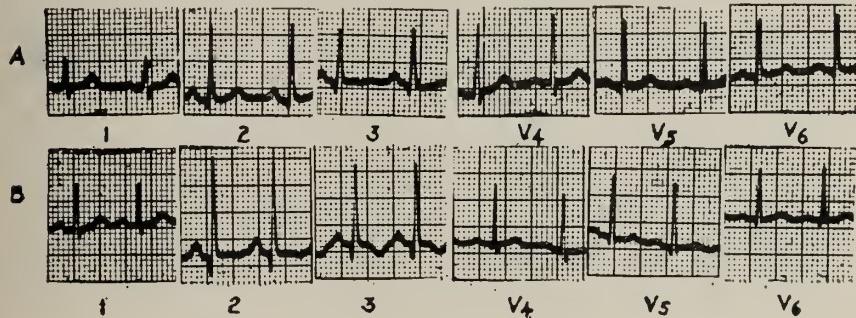
**Case 68** — A girl of 9 showed a perfectly normal electrocar-



**Case 68-P. B. Age 9 -Tonsillectomy. General anesthesia: Ether. A -before operation. Rate 94. B -after operation. Rate 135. Negative T waves. C - One week later. Rate 112-upright T waves.**

diagram before tonsillectomy which was performed under ether anesthesia. Following the operation the heart rate increased to 135 per minute and the electrocardiogram showed higher voltage of QRS complexes and negative T waves in Lead 111. One week later with a rate of 112 the T waves were upright again.

**Case 98** — A girl of 12 is similar to the previous one. A normal electrocardiogram with a rate of 105 was obtained before operation for bilateral strabismus performed under general an-



**Case 98-M. E. L. - Age 12 - Strabismus bilateral - General anesthesia.**

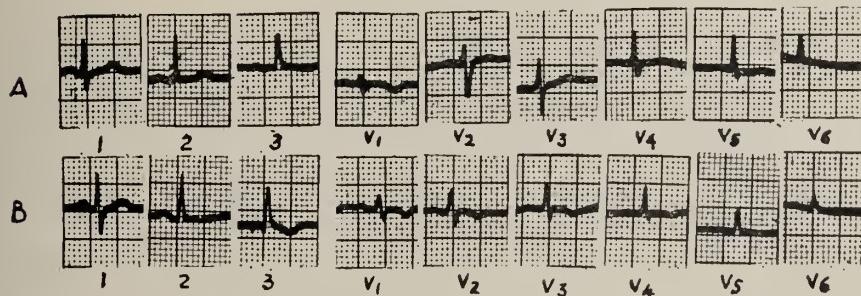
**A - before operation. Rate 105. B - after operation. Rate 130.**

**Negative T<sub>2</sub> and T<sub>3</sub>.**

esthesia. After operation, with a frequency of 130, T waves in Leads 11 and 111 became negative. A few days later the record returned to the original normal pattern.

The changes may be explained, at least in part, by the sinus tachycardia and the increased voltage of the QRS complexes.

**Case 86** — This was a 23 years old girl who received a general anesthesia for correction of a fractured clavicle. The pre-operative electrocardiogram was perfectly normal. Postoperatively T2 became isoelectric, T3 became deeper and negative T waves appeared in V1, V2, V3, and V4. These changes may be consistent



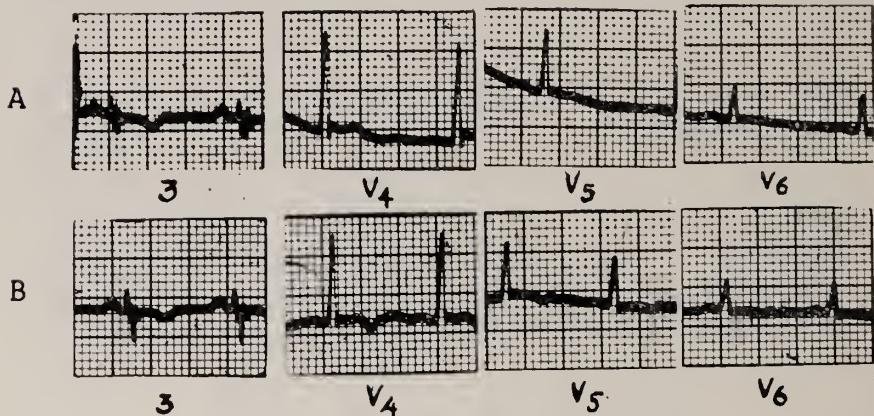
**Case 86-A. N. O. - Age 23 - Fractured clavicle. General anesthesia.**

**A - before operation - Rate 95. B - after operation - Rate 110.**

**Changes limited to T waves.**

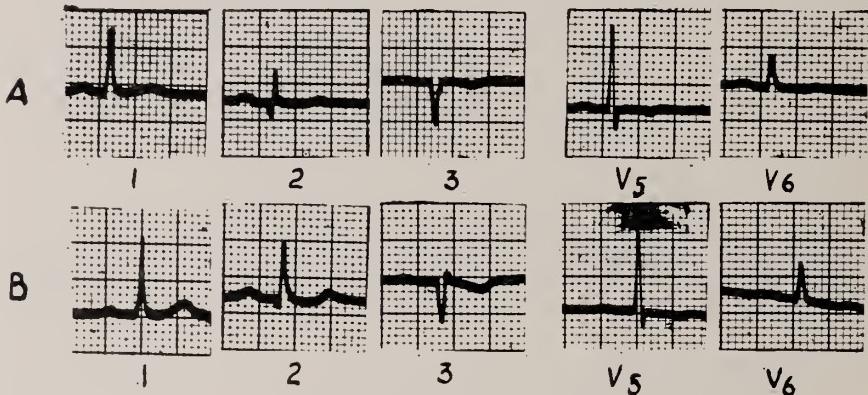
with a normal juvenile pattern which we know may appear or disappear in the same person.

**Case 99** — A young man of 29 was operated upon for hemorrhoidectomy under spinal and general anesthesia. Following the operation T waves became negative in V<sub>4</sub>, V<sub>5</sub>, and V<sub>6</sub>, but a week later T waves were again upright in all precordial leads.



**Case 99-L. W. - Age 29 - Hemorrhoidectomy. Spinal and general anesthesia. - A - Before operation. Rate 80. B - after operation. Rate 103. Negative T waves in V<sub>4</sub>, V<sub>5</sub> and V<sub>6</sub>.**

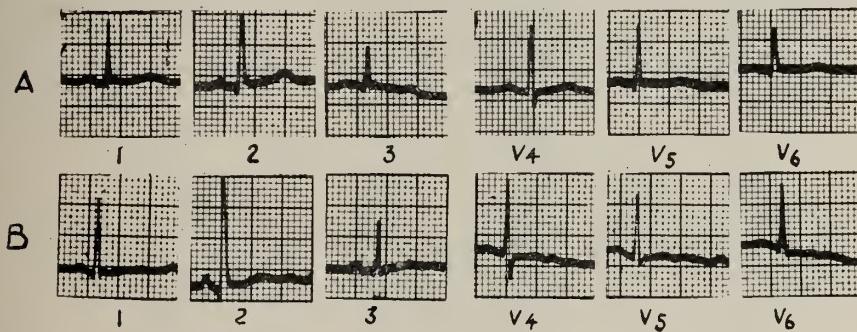
**Case 85** — A 74 years old man on whom a transurethral re-



**Case 85-M. B. A. - Age 74 - Transurethral resection of prostate. Spinal anesthesia. A - before operation. Rate 75. Old posterior myocardial infarct. B - after operation. Rate 58. Minimal changes in T waves.**

section was performed under spinal anesthesia. His original electrocardiogram showed a rate of 75 and suggested an old posterior or diaphragmatic myocardial infarct. The heart rate was 58 following the operation and showed only insignificant changes in the voltage of the T waves. He was discharged in apparently normal condition to die at his home about a week later of a cerebrovascular accident.

**Case 80** — A 49 years old woman was operated upon for cystocele and rectocele under Pentothal and spinal anesthesia. The



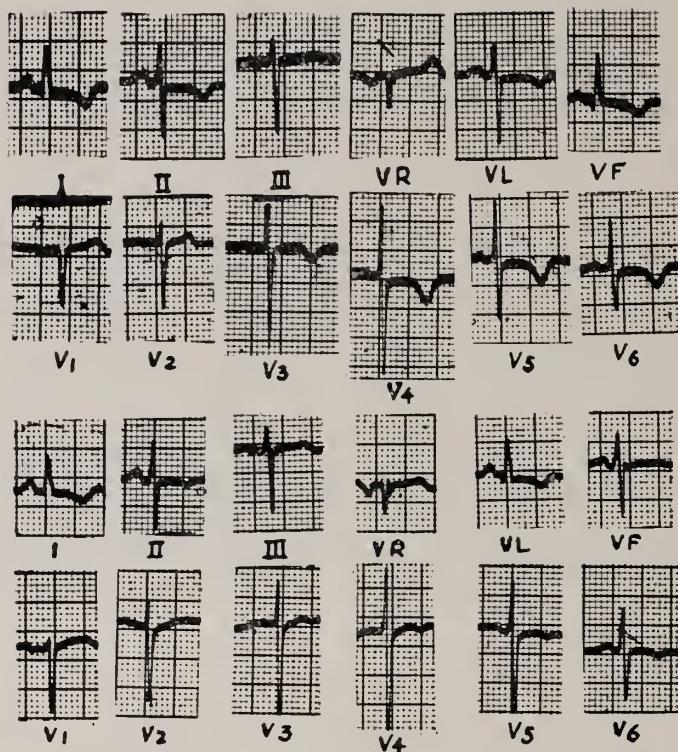
**Case 80-B.** B. R. — Age 49 — Cystocele and rectocele — Pentothal and spinal anesthesia. A — Before operation. Rate 65. B — after operation. Rate 92. Lower T<sub>1</sub> and negative T in V<sub>4</sub>, V<sub>5</sub> and V<sub>6</sub>.

postoperative changes observed in the electrocardiogram were minimal consisting of a low T<sub>1</sub> and slightly negative T waves in V<sub>4</sub>, V<sub>5</sub>, and V<sub>6</sub>.

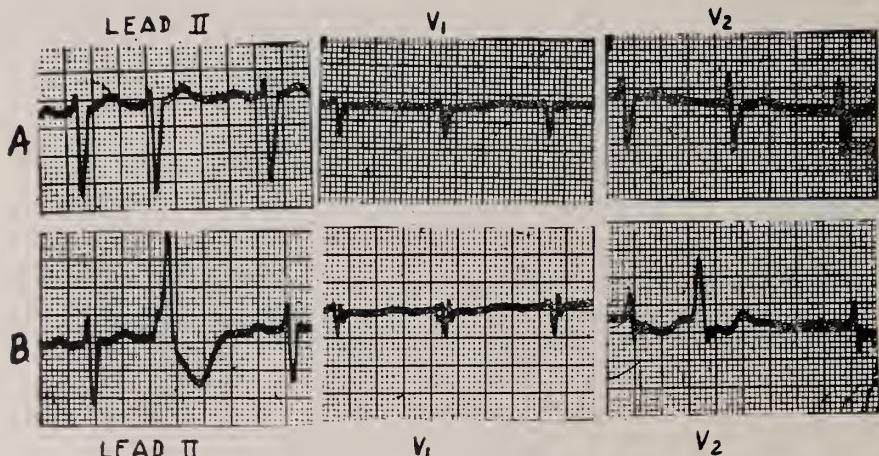
**Case 26** — A man of 64 on whom sympathectomy was performed under spinal anesthesia. His preoperative electrocardiogram was definitely abnormal. There were negative T<sub>1</sub>, T<sub>2</sub>, T in VL and VF and deeply inverted and symmetric T waves in V<sub>3</sub>, V<sub>4</sub>, V<sub>5</sub>, and V<sub>6</sub>. Postoperatively the changes in the T waves, if anything, were less pronounced. A similar pattern was evident, but there was definite waning of the T waves.

**Case 34** — An 87 years old man whose fractured neck of the femur was nailed under spinal anesthesia. His preoperative electrocardiogram showed right bundle branch block. His postoperative record revealed pulsus bigeminus as evidence of this old man's susceptibility to digitalis. He made an uneventful recovery.

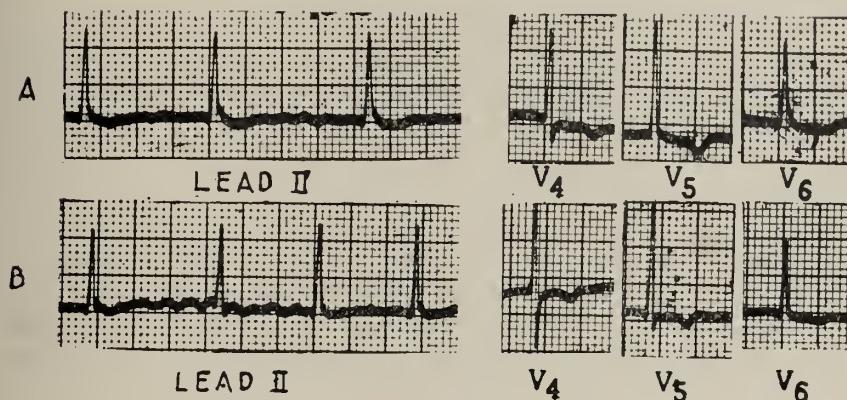
**Case 88** — A man 72 years old showing auricular fibrillation and digitalis effect underwent a transurethral resection of the prostate under spinal anesthesia. His postoperative electrocardiogram showed only less pronounced inversion of the T waves in the chest Leads.



**Case 26 - I. R. - Age 64 - Sympathectomy - Spinal anesthesia. A - before operation - Rate 64 - B after operation - Rate 100. Inversion of T waves less marked.**

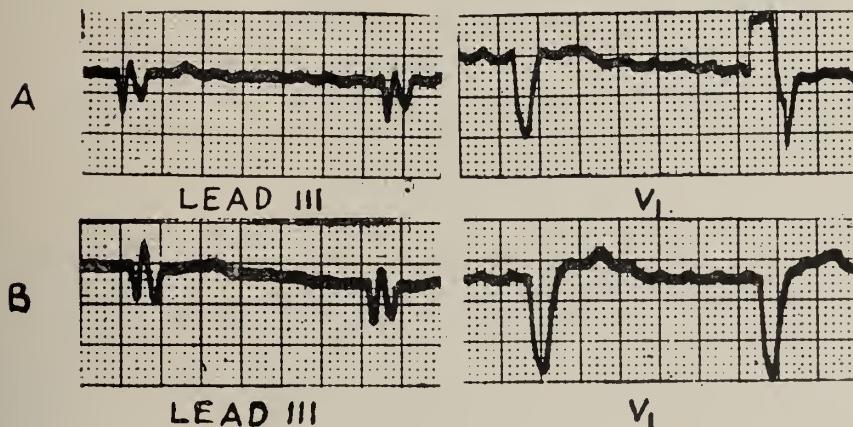


**Case 34 - J. L. C. - 87 - Fractured hip. Nail fixation. Spinal anesthesia. A - before operation. B - after operation. Pulsus bigeminus. Digitalis sensitivity.**



**Case 88-F.V. Age 72.** Transurethral resection of prostate. Spinal anesthesia. A - before operation. Auricular fibrillation. Digitalis effect. Rate 84. B - after operation. Rate 101. Less pronounced inversion of T waves.

**Case 39** — This 60 year-old man showing auricular flutter and bundle branch block preoperatively, claimed that his conduction defects were congenital in origin and that he came near death once when digitalis was administered. There were no signs



**Case 39-A. A. - Age 60 - Prostatectomy suprapubic. General anesthetic.** A - before operation. Rate 46 - Auricular flutter chronic and probably congenital and bundle branch block. B - after operation. Rate 53. No changes.

of congestive heart failure. Suprapubic prostatectomy was performed uneventfully and there were no electrocardiographic changes after surgery, except that his usual bradycardia of 46 increased to a rate of 53.

### Discussion

Dennis (1) and collaborators, from the Cardiovascular Research Center of Baylor University College of Medicine, reported on 8 patients who developed deep T wave inversions during the period immediately after operation or after anesthetization. These changes persisted for as long as several weeks in some patients. No laboratory or clinical evidences suggestive of myocardial necrosis or coronary disease were present.

Although two patients were over 50 years old, five were under the age of 40. Seven of the eight patients underwent minor operative procedures under light anesthesia. Pentothal was used as the preanesthetic agent for all, and succinylcholine, D-tubocurare, Anectine or Fluothane were used as adjunctive anesthetic agent. All but one patient exhibited a period of hypotension before the administration of vasopressor drugs (Neosynephrine, Aramine, or Levophed). Acute fulminating pulmonary edema without hepatomegaly or elevated jugular venous pressure was the initiating feature of the hypotension in four patients. The authors seem to suspect Pentothal as the primary causative element and the possible toxic role of this anesthetic is presently being investigated.

Howland et al (2) took routine postoperative electrocardiogram on 782 patients, of whom 321 (41%) had normal records. The electrocardiograms of the remaining 461 patients revealed either abnormalities of rate, rhythm, or conduction or myocardial changes suggestive of disease. Of these, 56 could have been detected by applying criteria representing the major cardiovascular problems encountered in the recovery room, 48 were detected by a preoperative electrocardiogram, and 167 were not detected prior to operation. However in all but two of the latter the abnormalities of the electrocardiogram resulted from chronic heart disease. It appears that changes that occur as the result of operative and postoperative medical and physiologic phenomena can be detected by recording postoperative electrocardiograms on patients showing marked bradycardia or arrhythmia, sudden unexplained tachycardia, hypoxia, or hypotension not amenable to restoration of circulating fluid volume. The authors did not deem necessary the routine postoperative electrocardiogram, but claimed that a routine preoperative electrocardiogram is indicated for every patient scheduled for operation.

Hurwitz (3) reported his studies in a series of 220 subjects, 150 of whom were known cardiac patients, 30 normals served as control. The various arrhythmias, changes in conduction and changes in ST-T segments were most frequently observed. His conclusions were that the over-all prognosis of cardiac patients undergoing surgery is good when carefully prepared and diligently watched postoperatively.

Of 192 patients with previous myocardial infarctions operated upon for transurethral resection, there were 9 deaths (4.7%) according to Thompson, Kelalis and Connolly.<sup>4</sup> All deaths were attributed to cardiovascular disease. Mortality rate, interestingly enough, was not related to the time interval between infarction and subsequent prostatectomy but was higher in the patients who had another recent major surgical procedure.

In our rather small series of 100 patients, there was not a single surgical death. The electrocardiographic changes were relatively insignificant and mainly limited to the T waves. Although several cases developed moderate to severe hypotension following operation, no case of acute pulmonary edema could be detected. The changes observed in the QTc ratio did not seem to influence one way or the other the clinical and postoperative course of the patients.

The T wave is the most labile part of the electrocardiogram. It is well known that its amplitude, duration, and polarity depend on two factors: the magnitude and direction of the QRS complex and the ventricular gradient. A change of either of these will result in alterations of the T wave.

There are numerous factors which may induce changes in the T waves. These are only a few of them: emotional factors, especially fear, sinus tachycardia, hyper and hypokalemia, administration of digitalis and quinidine, the level of serum calcium and the pH of the blood, meals or food intake, the juvenile pattern which may appear and disappear, the position of the exploring electrode and of course endocardial, epicardial and myocardial lesions.

Addendum — This report was finished in May this year. An interesting symposium on "Cardiovascular -- Pulmonary Problems Before and After Surgery" appeared in the October issue of the American Journal of Cardiology. "Postoperative Myocardial Infarction" is ably discussed by Simon Dack and "Electrocardiographic Changes Following Surgery" by Nejat Caginalp and Isidore Stein.<sup>5</sup> The "Summary and Conclusions" of this last paper reads as follows: "a study of 1,080 consecutively operated patients (none with cardiac surgery) revealed 51 (4.7%) with postoperative electrocardiographic abnormalities of various types. The ma-

jority of these patients were asymptomatic. Eleven of the 51 patients died, autopsies are reported in 4.

All the patients were operated on under cyclopropane or Fluothane general anesthesia, some for as long as four hours. Most of the surgery was performed for pathology of the abdominal viscera.

The electrocardiographic changes of various types of arrhythmias, conduction disturbances and changes of myocardial ischemia and infarction.

The serious electrocardiographic aberrations were correlated mainly with prolonged periods of hypotension during surgery.

Other factors such as electrolytes, blood volume, length of surgery and underlying coronary sclerosis may be operative, but their evaluation requires further study".

Interestingly enough the authors include among the illustrations a patient who had had chest pain for about 6 months before an esophagogastrectomy was performed and who developed supraventricular tachycardia and died. Another patient showed left bundle branch block and recent anterolateral wall infarction on the sixth postoperative day and still another showed increased P-R interval and complete right bundle branch block on the tenth postoperative day.

After having read those papers we found no reasons to alter in any way the summary and conclusions of our study as originally drawn.

#### SUMMARY AND CONCLUSIONS

1—We have studied the electrocardiogram taken before and shortly after operation on 100 consecutive surgical cases admitted to Hospital Mimiya. The youngest patient was 4 years old, the oldest 87. Grouped by age, there were 7 patients between 4 and 20 years; 22 between 21 and 40; 30 between 41 and 60 and 41 between 60 and 87. In this last group there were 7 octogenarians.

2—The postanesthetic electrocardiographic changes observed in this study were mainly limited to the T waves. The alterations were usually insignificant and transient.

3—We agree with Howland and collaborators that routine postoperative electrocardiogram are not justified, but that a pre-operative electrocardiogram is indicated for every patient scheduled for operation.

4—Postanesthetic or postoperative electrocardiograms should be limited to patients who show either during the operation or in the recovery room, marked bradycardia or arrhythmia, sudden unexplained tachycardia, hypoxia or hypotension not amenable to restoration of the circulating fluid volume.

5—Our studies confirm the fact that a markedly abnormal

electrocardiogram should not per se be a deterrent to necessary surgical intervention.

#### RESUMEN Y CONCLUSIONES

1. Hemos estudiado el electrocardiograma antes y poco tiempo después de la anestesia en 100 casos consecutivos admitidos al Hospital Mimiya. Las edades variaban entre 4 y 87 años. En el grupo de 4 a 20 años de edad había 7 pacientes, 22 en el grupo entre 21 y 40 años, 30 en el grupo entre 41 y 60 años de edad y 41 en el grupo entre 61 y 87 años. Siete eran octogenarios.

2. Los cambios encontrados con mayor frecuencia se limitaron a las ondas T y fueron transitorios e insignificantes.

3. Creemos como Howland y colaboradores que no está justificado el tomar rutinariamente electrocardiogramas postoperatorios, pero que un electrocardiograma preoperatorio sí está indicado en todo caso quirúrgico.

4. Electrocardiogramas postoperatorios se deben limitar a los enfermos que durante la operación o poco después de la misma demuestran una marcada bradicardia o arritmia, una taquicardia súbita e inexplicable, o hipoxia o hipotensión que no responden a la restauración del volumen circulante.

5. Nuestros estudios confirman el hecho de que un electrocardiograma anormal no es, per se, obstáculo para intervención quirúrgica necesaria.

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## SECCION DE RESUMENES

Editada por: RAFAEL G. SORRENTINO, M.D.

**ONE THOUSAND CASES OF PORTAL CIRRHOSIS OF THE LIVER** (Resumen de la experiencia clínica con mil casos de cirrosis portal hepática) Irving B. Brick, M. D. y Col. Eddy D. Palmer, M. D. Archives of Internal Medicine Vol. 113 — No. 4 — April 1964.

En este estudio, los autores presentan su experiencia con los casos de cirrosis portal haciendo énfasis en el desarrollo natural de la enfermedad y evalúan los métodos quirúrgicos usados hoy en día para tratar de corregir la hipertensión portal y las várices esofágicas.

Todos los casos fueron confirmados histopatológicamente por biopsia, durante laparotomía o en autopsia. Del total, 780 eran hombres y 220 mujeres. 882 presentaban cirrosis de Laennec y 118 eran de cirrosis postnecrótica. Había historial confirmado de alcoholismo en 745 de los casos. Había 104 casos con historial de hepatitis, 20 de los cuales presentaban cirrosis postnecrótica.

El problema más apremiante en los casos de cirrosis hepática es el del desarrollo de hipertensión portal y por consiguiente la aparición de várices en el esófago. Junto con el coma hepático, es ésta una de las causas de muerte más frecuentes en estos casos por su tendencia a sangrar.

Además de la presencia de várices esofágicas, en aproximadamente 30% de los casos de cirrosis hay lesiones en el tracto gastrointestinal que son puntos potenciales de hemorragia, principalmente, úlceras duodenales que ocurren en 10% de estos casos. De los mil pacientes estudiados, en 728 casos se descubrieron várices por medio de esogagoscopia. Estudios radiológicos, por el contrario, demostraron várices en sólo 27% de los casos.

Es interesante notar que en 174 pacientes escogidos para estudiar el comportamiento de las várices esofágicas, se demostró que éstas no guardaban ninguna relación con los cambios en el cuadro clínico de la cirrosis.

De los mil casos, 263 sangraron debido a várices esofágicas. De estos, 105 murieron y 110 se trajeron con decompresión portal por medio de anastomosis porta-cava o esplenorenal. Además de estos, hubo 62 casos en los cuales se hizo cirugía sin ellos haber sangrado. En 152, se utilizó la anastomosis porta-cava y en 29 la esplenorenal. Las indicaciones para cirugía eran únicamente; la presencia de várices esofágicas en un paciente cuya cirrosis estaba estable con una compensación hepática más o menos buena. Los autores son de opinión que la mera presencia de várices esofágicas es un riesgo tan grande para el paciente, que se debe hacer cirugía una vez que la condición hepática así lo permita. En los 62 casos en que se intervino profilácticamente no se registraron hemorragias durante un período postoperatorio de más de 12 años y hasta la fecha todos viven. De 90 pacientes que sufrieron decompresión portal después de haber sangrado de várices una o más veces, 79 no han vuelto a sangrar durante un período máximo postoperatorio de 10 años. Es la experiencia de los autores que cuando se hace cirugía de emergencia debido a hemorragia masiva e incontrolable, la mortalidad operatoria es de 50%.

Del total de pacientes operados; 4.1% murieron durante el procedimiento o durante la primera semana postoperatoria. 11.0% murieron durante el primer mes. Luego de un término de 6 meses a 12 años, 80 pacientes han muerto y 92 viven.

El comportamiento de las várices esofágicas luego de la operación fue

estudiado por medio de esofagoscopías repetidas en 119 pacientes. En 70 casos las várices desaparecieron por completo. En 10 casos éstas desaparecieron pero recurrieron en un término de 1 mes a 9 años; en 39 casos no hubo cambio alguno en las várices.

Solamente se pudieron estudiar 310 casos hasta su muerte. En todos los casos se hizo autopsia excepto a 49. De los casos no operados, 31 murieron de causas no relacionadas a su condición hepática, y 199 debido a causas secundarias a su cirrosis especialmente a causa de hemorragias masivas de várices esofágicas, 105. De los casos operados, 80 murieron; 52 debido a fallo hepático y los 28 restantes, de causas ajenas a su enfermedad primaria.

A manera de comparación los autores presentan 60 casos de Schistosomiasis. 30 debido a *S. mansoni* y 30 debido a *S. japonicum*. En el total de 60 casos, várices esofágicas se descubrieron en 16; 5 de los cuales tuvieron hemorragias. 5 casos fueron operados sin mortalidad alguna y hasta el presente todos los 60 casos están con vida.

De la información dada por estos autores, uno puede concluir que el caso ideal de cirrosis hepática que más se puede beneficiar por procedimientos quirúrgicos encaminados a disminuir la hipertensión portal es aquel que apesar de tener várices esofágicas, nunca ha sangrado y su reserva hepática todavía es bastante buena. Aún en los casos que ha habido una hemorragia o más debido a várices, todavía se puede pensar en cirugía como un método bastante efectivo para prevenir una futura hemorragia mortal. En los casos de Schistosomiasis, la fisiopatología parece ser distinta y mayor número de casos se deben estudiar antes de dar una opinión en cuanto al tratamiento de la hipertensión portal que se desarrolla en estos casos.

CARLOS E. GIROD, M.D.

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**AN EXPLANATION FOR ABNORMAL WATER RETENTION AND HIPO-OSMOLALITY IN CONGESTIVE HEART FAILURE (Una explicación para la retención anormal de agua e hipoosmolalidad en desfallecimiento cardíaco congestivo) By Bell, Schede and Bartter; The Amerian Journal of Medicine Vol. 36; March 1964; No. 3.**

Estudios de excreción de agua, sodio y potasio en once sujetos normales y cinco pacientes con fallo cardíaco derecho revelaron que los pacientes en fallo:

1—re establecieron el umbral renal de excreción de agua después de una antidiuresis producida por Pitresina pasado un intervalo de tiempo igual al observado en los sujetos normales.

2—Demostraron una habilidad limitada para excretar sobrecarga de agua administrada tanto oral como intravenosamente.

3—excretaron alguna agua después de cada sobrecarga de agua.

4—aumentaron la excreción de agua con la administración de manitol.

La filtración glomerular no era anormalmente baja en estos pacientes.

Los hallazgos sugieren que la inhabilidad para excretar agua y sodio en estos pacientes no fue secundaria a la hormona antidiurética y sí a un aumento en la reabsorción del filtrado glomerular en el túbulo proximal, de tal manera que cantidades limitadas de agua y sodio llegan al túbulo distal. Manitol actúa llevando sodio y agua al túbulo distal y como resultado se puede generar agua para excreción.

También se concluye por otras observaciones que aldosterona puede ser la causa de edema en algunos pacientes en fallo pero no en todos. La ausencia

de hipopotasemia en estos pacientes a pesar de niveles anormalmente elevados de aldosterona es evidencia de que la excesiva reabsorción de sodio debe ocurrir antes del túbulo distal que es donde se intercambió sodio por potasio.

JOSE PEREYO, M.D.

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**MASSIVE BLOOD REPLACEMENT WITHOUT CALCIUM ADMINISTRATION**  
(Transfusiones masivas de sangre sin administración de calcio) W. S. Howland,  
O. Schweitzer, C. Paul Sayan: *Surg., Gyn. and Obst.* 118 #4: 814-818, April  
1964.

Los autores ponen en duda la existencia de intoxicación por citrato al administrar dosis masiva de sangre anticoagulada con solución de citrato ácido y dextrosa. Se teorizaba que el citrato se combina con el calcio iónico en la sangre y produce los síntomas de hipocalcemia. Ellos estudiaron 872 pacientes a quienes se les administró 5 ó más unidades de sangre durante la operación o en la unidad de cuidado intenso sin administrársele calcio. De estos pacientes hubo 20 muertes, y todas con más de diez transfusiones. Trece de ellas fueron debido a hemorragia incontrolable, y siete (7) a defectos específicos de coagulación que no se hubieran corregido con administración de calcio. El nivel de calcio más bajo que se obtuvo fue de 8.4 mg. %.

Al repasar las muertes ocurridas en un período de tiempo anterior a este, cuando todavía se administraba calcio en estos casos, encontraron 20 muertes por fibrilación ventricular.

En la discusión estos investigadores mencionan estudios previos donde indican la toxicidad de calcio para el miocardio lipóxico causando fibrilación ventricular. También llaman la atención a otros estudios donde se le administraba EDTA a pacientes con arritmias cardíacas con el propósito de bajar el calcio sanguíneo, y lo único que consiguieron fue suprimir una que otra contracción ventricular prematura, prolongar el segmento Q-T en el electrocardiograma, y producir una ligera hipotensión, a pesar de lograr concentraciones de calcio de 7.1 mg. %.

Concluyen el artículo diciendo que, ya que no hay evidencia para decir que la administración de calcio es beneficiosa en estos casos, y que hay una posibilidad de que haga daño, recomiendan que no se le inyecte esta substancia a estos pacientes.

GERHART RAMIREZ SCHON, M.D.

— — —

**HEPATIC PHYSIOLOGIC AND MORPHOLOGIC ALTERATIONS IN HEMORRHAGIC SHOCK** (Alteraciones morfológicas y fisiológicas del hígado durante "shock" hemorrágico) W. C. Shoemaker, P. B. Szanto, L. B. Fitch, N. R. Brill, *Surg. Gynec. and Obst.* 118 #4:828-836, April 1964.

Estos investigadores han estudiado las alteraciones en la microcirculación del hígado en ratas, ratones y perros, y compararon estas alteraciones fisiológicas con los cambios morfológicos de animales y humanos que murieron bajo condiciones similares. Para estudiar la microcirculación se usó un sistema de lentes que aumentaba hasta 250 veces el tamaño original y el "shock" se producía renoviendo sangre del animal hasta que le bajara la presión en tre 40 y 60 milímetros de mercurio. Se observó esta secuencia de eventos en todos los animales: (1) Agregación de células rojas en los sinusoides; (2) Dilatación de las venas centrales a medida que se formaban agregados más grandes; (3) Marcada dilatación de los sinusoides cerca de las venas centrales con compresión de las células hepáticas adyacentes; (4) Disminución marca-

da del flujo sanguíneo a medida que ocurría más congestión sinusoidal; y (5) Paro total del flujo sanguíneo en todos los vasos.

Se obtuvieron biopsias hepáticas a medida que se producían los cambios anteriores y los cortes se pudieron clasificar en tres estados de dilatación y congestión central con compresión y necrosis centrolobular. Cambios similares se notaron en cortes de hígado de autopsias de humanos muertos en "shock" hemorrágico o traumático.

Concluyendo, los autores aciertan que esto es suficiente evidencia para asumir que la congestión aguda de los sinusoides hepáticos representa la lesión morfológica y la base funcional para el desarrollo del cuadro clínico de "shock" hemorrágico irreversible.

GERHART RAMIREZ SCHON, M.D.

— — —

**THE CARDIAC DISEASE ASSOCIATED WITH THE CARCINOID SYNDROME**  
(Carcinoid Heart Disease) (La Enfermedad Cardiaca Asociada al Síndrome Carcinoide (Enfermedad Cardíaca Carcinoide)) William C. Roberts and Albert Sjoerdsma, National Institute of Health, Bethesda, Maryland The American Journal of Medicine, Vol. 36. No. 1, January 1964.

En un estudio detallado los autores describen nueve pacientes llevados a autopsia en los cuales los hallazgos eran típicos de enfermedad cardiaca carcinoide. También presentan ocho casos de pacientes con el Síndrome Carcinoide pero sin enfermedad cardíaca. Desde el punto de vista de la clínica, la enfermedad cardíaca carcinoide se caracteriza por un soplo cardíaco sugestivo de estenosis de la pulmonar o de insuficiencia tricuspidea. Los demás hallazgos físicos, los Rayos X, y el electrocardiograma no nos ayudan mucho en establecer el diagnóstico. Patológicamente el proceso se caracteriza por el depósito de un tipo peculiar de tejido fibroso, que no contiene fibras elásticas, en el endocardio de las valvas valvulares, el endocardio de las paredes de las cavidades y en la íntima de los grandes vasos. Es interesante notar que el proceso se extiende más extensamente por la aurícula derecha que por el ventrículo y que predominantemente las lesiones se encuentran en el lado derecho del corazón. Cuando hay lesiones en el lado izquierdo es porque ya está afectado el derecho. Los autores no describen ningún caso con lesiones únicamente en el lado izquierdo ni aún cuando se descubren defectos comunicantes entre corazón izquierdo y derecho. Cómo y por qué estos depósitos se forman sigue siendo un interesante misterio el cual los autores lo discuten ampliamente. Se incrimina de alguna forma u otra a la serotonina pero no hay nada concreto. En un aníplico apéndice al artículo los autores nos presentan todos y cada uno de los nueve casos con un breve historial clínico y un resumen de los hallazgos de autopsia. El artículo nos presenta unas excelentes fotografías de los hallazgos tanto macro como microscópicos.

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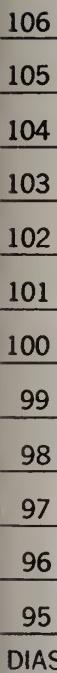
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1. Mann, Hubert, M.D., Journal of the Mount Sinai Hospital, New York, May-June, 1956.

2. Huppert, V., M.D., and Boyd, L. J., M.D., F.A.C.P., Bulletin, New York Medical College, Flower and Fifth Avenue Hospitals, New York, May, 1956.

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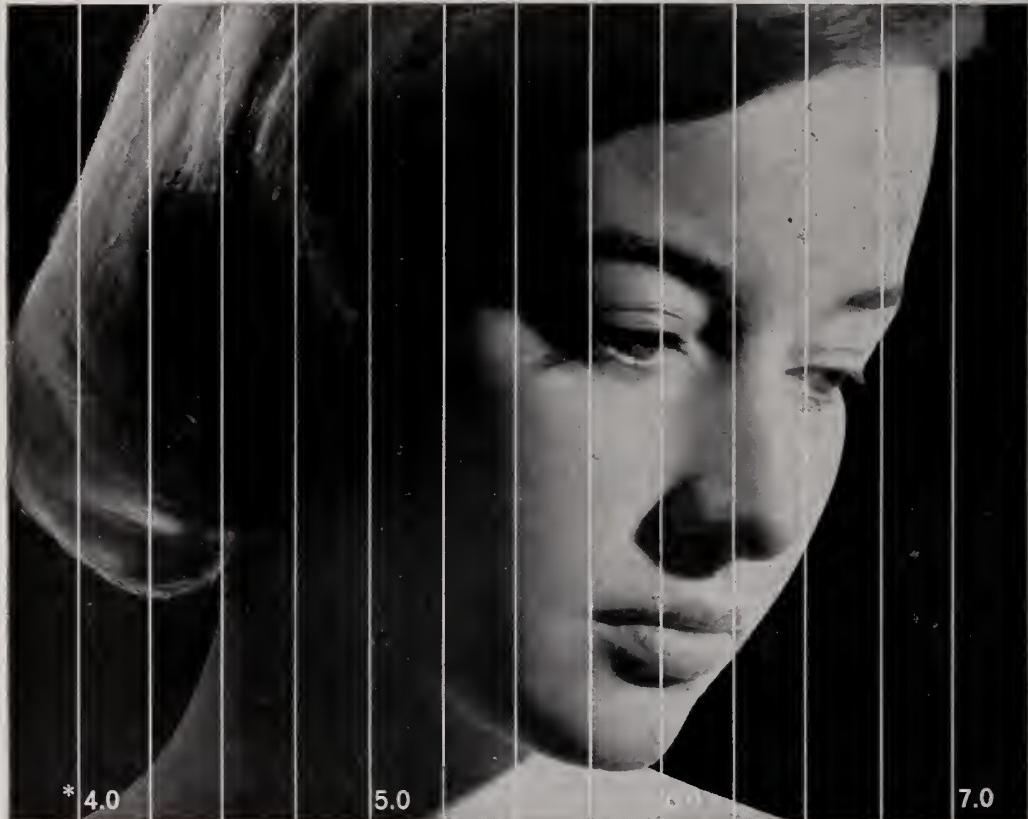


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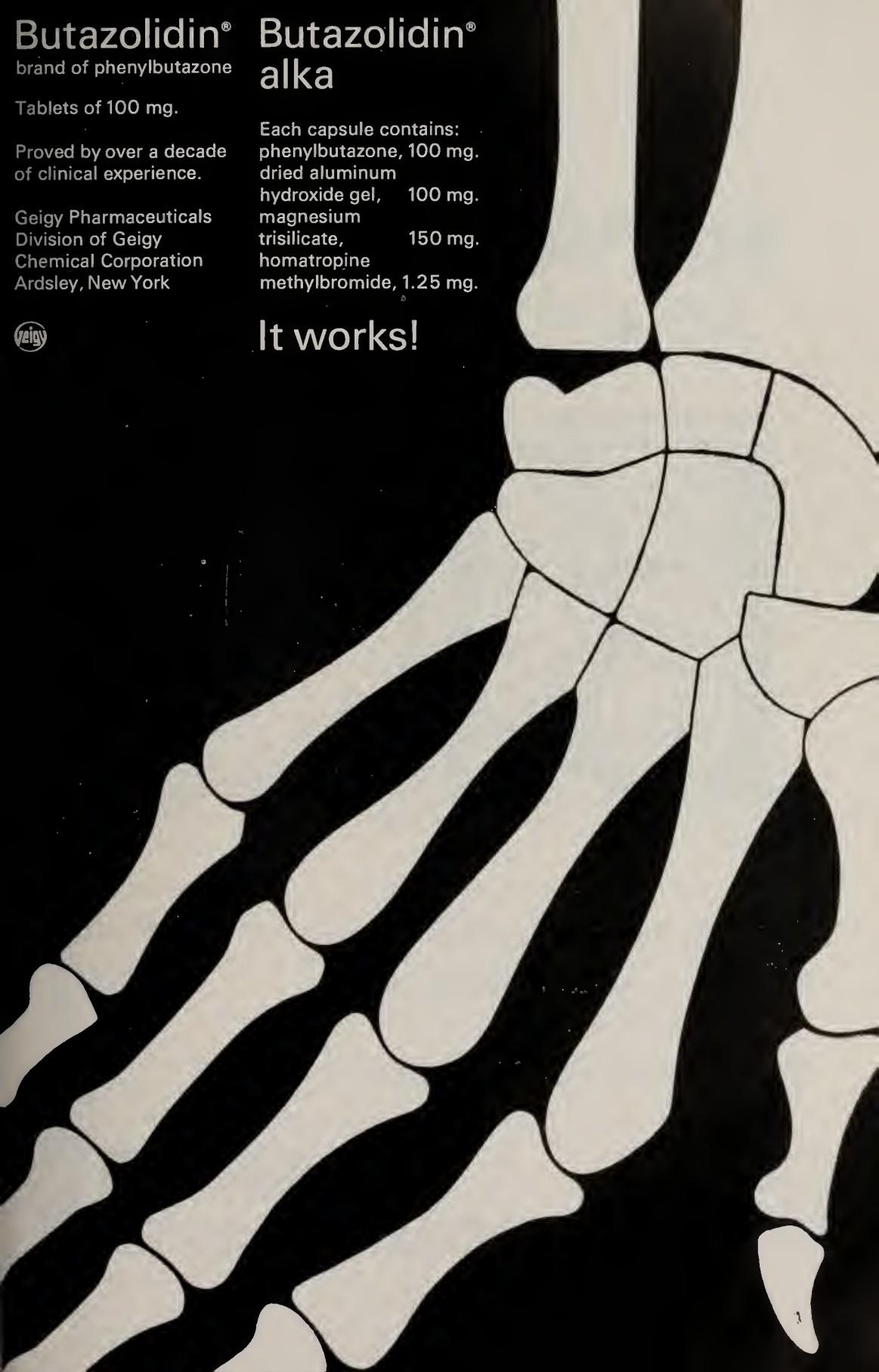
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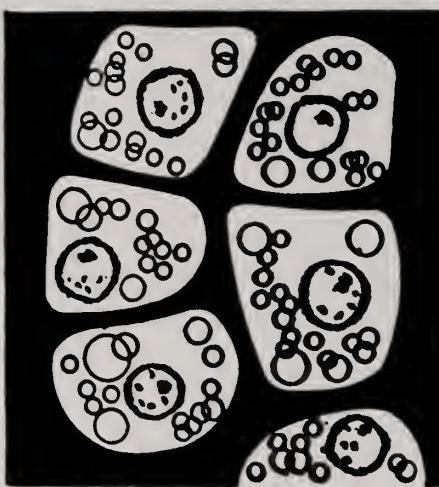
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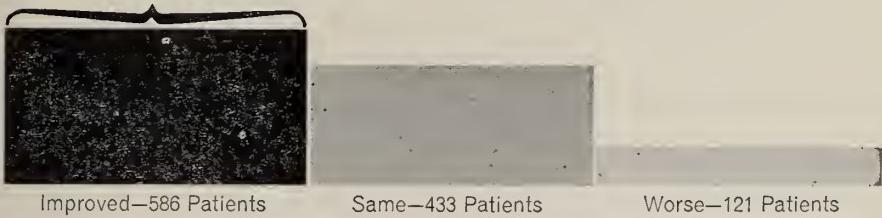
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# BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO

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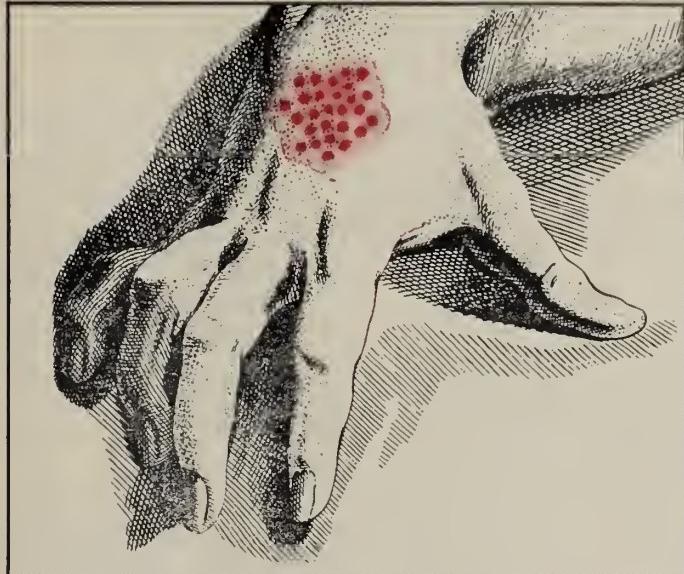
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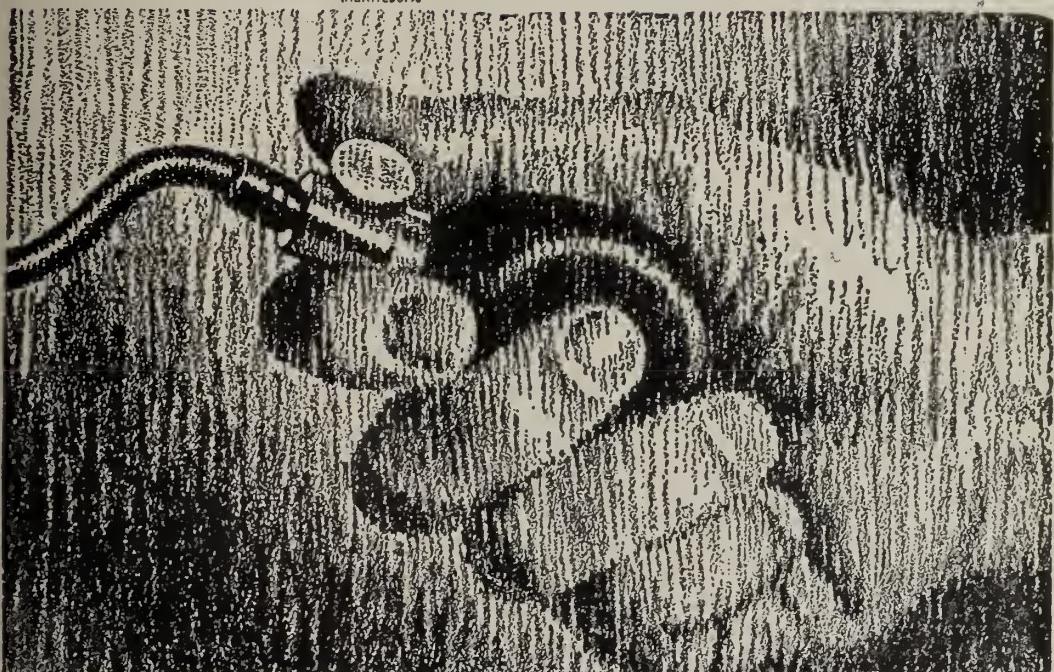
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hypertension

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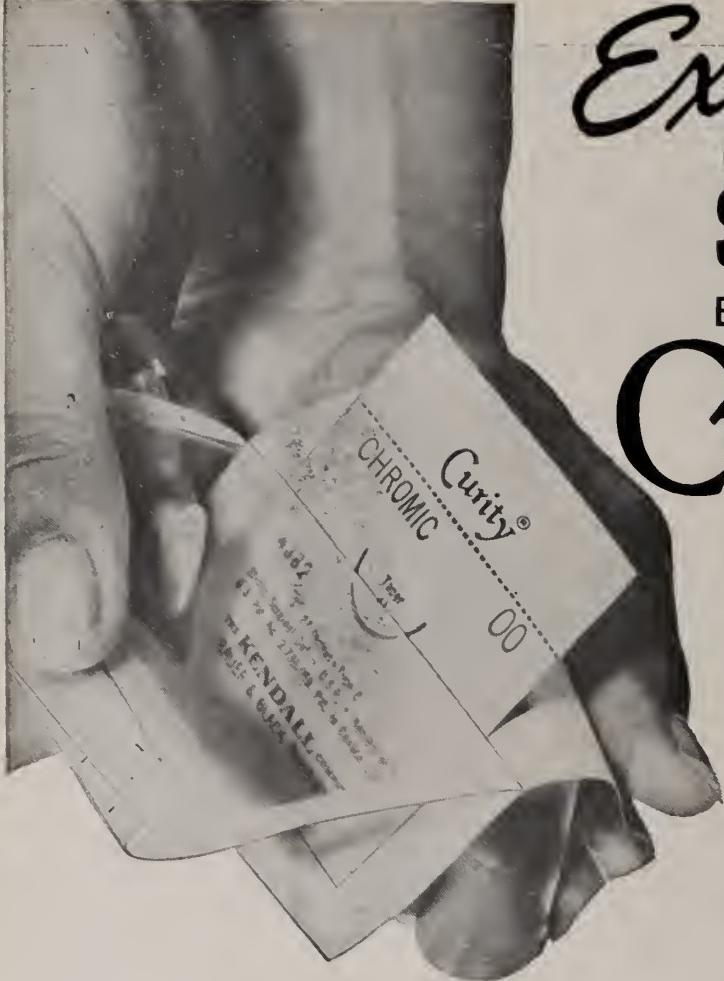
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<sup>f</sup>Mean Blood Pressure—½ pulse pressure plus diastolic pressure.

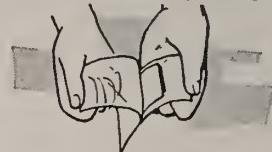




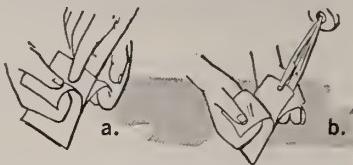
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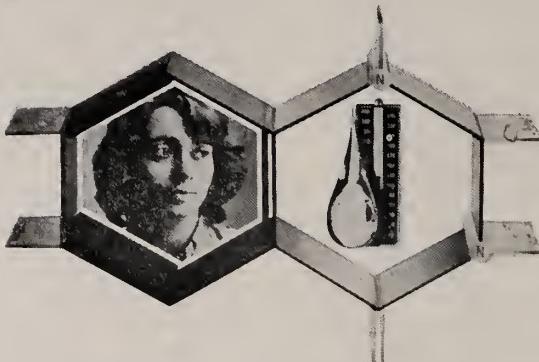
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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



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## POST PRANDIAL SERUM TURBIDITY IN THE DETECTION OF IMPAIRED FAT ABSORPTION

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Supported in part by Baxter Laboratories, Inc., Morton Grove, III.

The detection of impaired digestion or absorption of fats is of interest in many clinical situations including diseases of the small intestine, biliary tract, and pancreas and in the evaluation of nutritional problems which may follow certain surgical procedures. Although the presence of steatorrhea can often be suspected clinically, a considerable amount of fat may be present in the feces in the absence of diarrhea.<sup>1</sup> Laboratory confirmation of the presence or absence of malabsorption of fats is thus often necessary.

Clinical application of methods for measuring absorption of lipids has been restricted by technical difficulties or special facilities required. Although the quantitative determination of fecal fat under controlled conditions is the most direct method for the detection of steatorrhea,<sup>2</sup> practical considerations, such as the need for dietary control and the collection and processing of feces for several days limit the clinical application of this method. These have lead to the search for other methods which often have involved the examination of blood, urine or fecal collections after a test meal.

Vitamin A, a fat soluble vitamin, has been used as a test of fat absorption but its use is objectionable because of the fact that it is not a lipid. The laboratory determination is not without

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\* From the Radioisotope and Medical Services, Veterans Administration Hospital, San Juan, Puerto Rico; and the Departments of Biochemistry and Nutrition and Medicine, University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

pitfalls. Although measurement of lipids labelled with radioisotopes have proven their clinical worth<sup>1,3,4</sup> measurement of fecal loss, which is the most reliable parameter, requires stool collection for several days. The facilities of a radioisotope laboratory are also required.

Serial determination of blood levels of lipids following a fat meal provide an index of the rate of absorption from the intestinal tract.<sup>5</sup> Quantitative methods for determination of blood lipids are, however, difficult and time consuming.

The bulk of the absorbed lipid appears in the blood as protein coated triglyceride particles (chylomicrons) which make the plasma opalescent.<sup>6</sup> Attempts to devise accurate techniques for estimating the concentration of these particles have been only partially successful.<sup>7,8</sup> The methods require considerable technical skill and are not always reproducible. An alternate method takes advantage of the scattering effect which these particles cause on a beam of light passing through their suspension in plasma. The scattering effect is proportional to their numbers and size. Measurement of reflected (nephelometry)<sup>7,8</sup> or of transmitted light (optical density, turbidity)<sup>9,10,11</sup> provide indices of the concentration of fat. By using an appropriate filter the interference by colored substances or by other macromolecules in the plasma can be minimized. These methods have been used fairly widely for the detection of impaired fat tolerance in patients with atherosclerosis and other conditions,<sup>10,12,13</sup> but their use as tests for fat absorption has not been frequently reported.<sup>5,11,15</sup>

#### Materials and Methods:

Fifty nine males were studied. The diagnostic categories are given in Table I. The "normal" subjects included 5 healthy hospital employees and 5 ambulatory patients hospitalized for conditions which do not affect gastrointestinal or metabolic processes. The patients with myocardial infarction had had their acute episodes not less than 3 months before the test and were ambulatory and free of congestive heart failure. The diagnosis of sprue was based on the usual clinical criteria and the abnormality of at least two tests of intestinal absorption (d-xylose, vitamin A, vitamin B<sub>12</sub>). In all patients who had gastrectomy the operation had been performed because of duodenal ulcer.

Following an overnight fast, a 10 ml blood sample was drawn and placed in a tube containing 0.15 ml of saturated solution of potassium oxalate. A test meal consisting of 350 ml of 18% cream

TABLE I -- CASES STUDIED

Diagnosis	Number	Steatorrhea
Normal	10	0
Myocardial Infarction	4	0
Tropical Sprue	15	13
Liver Disease	2	0
Schistosomal, 1		
Laennec's, 1		
Pancreatitis	3	1
Chronic insufficiency, 2		
Acute in remission, 1		
Small Bowel Disease	8	2
Non-specific enteritis, 5		
Thrombosis mesenteric veins, 1		
Leukemia, 1		
Fatty infiltration of mesentery, 1		
Thyrotoxicosis	2	1
Gastrectomy	15	10
	59	27

(63 g of fat), approximately 25 uc of radioiodinated triolein\* and 20 g of barium sulfate suspended in water was then given. Oxalated blood samples were drawn 2, 4, 5, 6 and 8 hours after the test meal. Water, but no food was allowed until after the last blood sample was obtained. Physical activity was not restricted. The completeness of gastric emptying was determined by roentgenogram 4 hours after the ingestion of the test meal. Feces were collected for at least 72 hours. Total and lipid radioactivity was determined in each blood sample. Fecal radioactivity was determined in all cases as described elsewhere.<sup>3</sup> Blood radioactivity levels were expressed as percentage of the administered dose per liter of blood (% A.D./L). Total fecal fat was determined by Van de Kamer's method<sup>2</sup> in thirty seven patients.

Determinations of plasma turbidity were performed as follows: Blood samples were spun for 10 minutes at 2,000 RPM. The plasma was removed and read in a Beckman DU spectrophotometer using 10 x 48 mm silica cells with a 10 mm light path. Readings were taken at a wavelength of 650 mu where the possible effects of hemolysis on light absorption were minimal. Isotonic saline was used as a blank. Changes in turbidity, expressed in optical density (O.D.) units were calculated using the turbidity of the fasting sample of plasma as reference.

### Results:

Plasma turbidity in the fasting state usually ranged from

\* Supplied by Volk Radiochemical Company, 8260 Elmwood Avenue, Skokie, Illinois.

0.050 to 0.150 turbidity units, but rarely was as high as 0.200 units. Two hours after the fat meal an increase in plasma turbidity was usually apparent which was maximal by the 4th, 5th or 6th hour.

Table II summarizes the data. The patients have been grouped into 4 categories according to the presence or absence of abnormal fecal excretion of radioactivity or fat. Because of

TABLE II — POSTPRANDIAL TURBIDITY

	Number of Cases	Maximum Turbidity Increment (mean $\pm$ S.D.)	Statistical Significance (p)
No steatorrhea	25	0.574 $\pm$ .313	Highly significant
Steatorrhea	17	0.164 $\pm$ .157	( $< 0.001$ )
Gastrectomy			
No steatorrhea	5	0.475 $\pm$ .233	Not significant
Steatorrhea	10	0.306 $\pm$ .230	( $> 0.5$ )

the expected influence of rapid gastric emptying on the postprandial lipemia levels, gastrectomized patients have been considered separately. Maximal turbidity, whether it occurred in 2 (one case), 4 or 5 hours, is shown. Although peak of turbidity was reached in the sixth hour in a considerable number of patients (nineteen cases), we have not used these values in this table because of two reasons; the levels did not appear to be appreciably higher than those of the fifth hour and because it seems likely that variables other than absorption may have influenced the turbidity levels at this time.

Among twenty five subjects without gastrectomy who had normal fecal radioactivity or fat excretion the maximal increment in turbidity averaged  $0.574 \pm 0.313$  O.D. units (mean  $\pm$  S.D.).

Two patients with tropical sprue had low turbidity values (peak: 0.107 and 0.221 units) in the absence of increased radio-triolein or total fat fecal loss. These cases are not included in the no-steatorrhea group above. Blood radioactivity peak levels in these individuals were also low, 1.6 and 2.1% A.D./L. respectively.

Maximal plasma turbidity in seventeen patients without gastrectomy who had abnormally high fat or radioactivity excretion averaged  $0.164 \pm .157$  O.D. units. These values differ significantly from that found in the first group ( $p < .001$ ).

Figure 1 summarizes the data from groups 1 and 2 in graphic form. If an arbitrary limit for normalcy of 0.250 units (approxi-

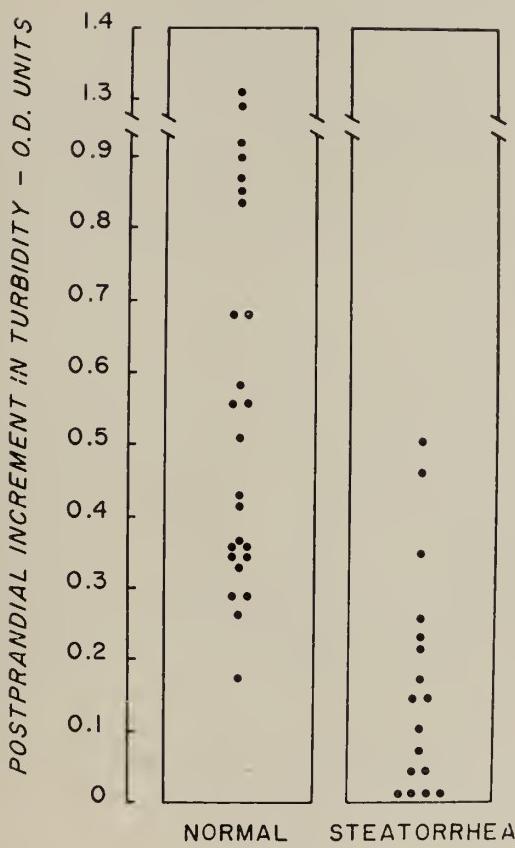


FIGURE 1

Values for maximal turbidity increments in patients without (left) and with steatorrhea (right). Mean values in each group indicated by bar.

mately one standard deviation below the mean) is chosen, it can be seen that only 4 patients with steatorrhea not due to gastrectomy show peak levels above this limit. The absorptive defect was slight in all these subjects (fecal triolein under 12% AD and stool fat under 14 g per day).

Five patients with gastrectomy did not have steatorrhea. Their maximal postprandial turbidity averaged  $0.475 \pm .233$  O.D. units. For the 10 who had steatorrhea the corresponding value was  $0.306 \pm .230$  O.D. units. The turbidity peak was less than 0.250 O.D. units in only 5 of this group. The difference between the gastrectomy group with and the one without steatorrhea is not statistically significant ( $p > 0.5$ ).

#### Discussion:

Blood levels of lipids after the ingestion of fat meal depend

both on the rate of mucosal absorption and the speed at which the fat is cleared from the blood into the body tissues.<sup>5</sup> The rate of absorption depends upon the rate of gastric emptying, the action of digestive enzymes and the functional capacity of the intestinal mucosa. Even though blood levels reflect factors other than absorption and they cannot measure closely total fat absorption a fairly good correlation with the amount of fecal fat was demonstrated by Drube and Giesecke in 30 normal and 23 patients with steatorrhea.<sup>15</sup>

The results of this study confirm the finding that measurement of the turbidity imparted to plasma by chylomicrons after a fat meal is a fairly reliable method for the detection of impairment of fat absorption due to disease of the small bowel. In the majority of patients where this was present, plasma turbidity was less than that seen normally. It is likely that this method is equally applicable to the diagnosis of cases of steatorrhea due to pancreatic disease.<sup>11,13</sup>

In two patients with sprue low levels of postprandial turbidity were observed in the absence of increased fecal excretion of fat or radioactive triolein. We believe that this finding reflects decreased mucosal absorption rates which are not detected by the excretion studies.

The fact that several patients with gastrectomies who had steatorrhea showed normal postprandial lipemia is not surprising. A similar finding when radioactive triolein was used has been reported.<sup>11</sup> Steatorrhea in these patients is related in part to reduced area and time of contact of the fat meal with the mucosa of the upper portion of the small bowel where most of the absorption of lipids occurs.<sup>16</sup> No functional defect of the mucosa exists so that the rate of absorption is not decreased. This method is therefore not useful in the detection of impaired fat absorption in gastrectomized patients.

On the other hand, delayed gastric emptying occasionally postponed the onset or decreased the degree of postprandial turbidity suggesting that impaired absorption was present. This factor affects any test which depends on the use of a test meal, especially one rich in fat.<sup>17,18</sup>

Although in this study five blood samples were taken after the test meal such repeated sampling is not needed for the usual clinical purposes. The two-hour sample is not as a rule informative. Chylomicron levels after the fifth hour may be particularly influenced by factors other than absorption, such as metabolic derangements, age and exercise.<sup>7,19</sup> A fasting sample and one taken 4 or 5 hours after the fat meal will usually suffice for the detection of impaired absorption. When a significant increase in turbidity is not detected it is useful to obtain an additional

sample in order to rule out the effect of slow gastric emptying.

In this study we have used a Beckman DU spectrophotometer for the turbidity measurements. These, however, can be made with any type of photometer such as the less costly Klett-Summerson or Coleman models provided the right type of filter (approx. 650 mu) is used.<sup>11</sup>

We believe that this procedure is more satisfactory than others currently being used as a qualitative test for impaired fat absorption and it therefore deserves wider clinical application.

#### SUMMARY

Serial measurements of plasma turbidity (optical density) after a meal consisting of 63 g of fat in the form of cream were made in fifty-nine persons, twenty seven of whom had impaired absorption of fat as detected by chemical determination or excretion of radioactive triolein. Postprandial turbidity increased more than 0.25 O.D. units in all but one thirty two persons showing normal fat absorption. Turbidity curves usually were found to be lower when steatorrhea due to intestinal or pancreatic disease was present. When steatorrhea was due to the presence of gastrectomy plasma turbidity levels were frequently normal. This method is recommended for use as a clinical test for the detection of impaired absorption of lipids due to disease of the small intestine or the pancreas.

#### RESUMEN

Se llevaron a cabo determinaciones seriadas de la turbidez plasmática (densidad óptica) después de la ingestión de 63 g de grasa en forma de crema en 59 personas, 27 de las cuales tenían un defecto de absorción de grasas comprobado por el examen químico de las heces o la excreción de trioleína radioactiva. Se registró un aumento en la turbidez plasmática de más de 0.25 unidades de densidad óptica en 31 de 32 individuos cuya absorción era normal. Las curvas de turbidez eran más bajas cuando se encontró esteatorrea debido a enfermedad intestinal o del páncreas. Cuando la esteatorrea se debía a la presencia de una gastrectomía la turbidez plasmática post prandial era a menudo normal. Se recomienda este método como prueba clínica para la detección de disturbios de absorción de lípidos debido a enfermedad del intestino o del páncreas.

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## **CONSIDERACIONES PRACTICAS SOBRE EL DIAGNOSTICO Y TRATAMIENTO DE LAS SORDERAS**

*NELSON FERNANDEZ-BLASINI, M.D.\**

### **INTRODUCCION**

Probablemente la sordera es una de las condiciones de más incapacidad emocional, sufridas por la raza humana. El recién nacido que es sordo de nacimiento aprende a hablar sólo con el más intenso entrenamiento y permanece de seis a ocho años de retraso en comparación con el resto de sus compañeros.

La persona que más tarde en la vida padece de "sordera" vive en un mundo de distorsión de sonidos, o aún de silencio. Así, privado de su medio primario de comunicación, tiende a retrajerse del mundo y vivir dentro de sí mismo.

Si queremos prevenir estas consecuencias de la pérdida de audición, es necesario un diagnóstico temprano; antes preferiblemente a que el infante sea tratado como retardado mental, que el niño falle en su trabajo escolar o el adulto pierda su empleo o se convierta en un recluso parcial.

Es pues, el propósito de esta comunicación repasar brevemente algunas de las causas de sordera, algunas pruebas de audición y algunas de las técnicas modernas de tratar esta condición.

### **PRUEBAS AUDITIVAS**

Un diapasón no es costoso. Su uso toma menos de un minuto. Diferencia la sordera conductiva de la perceptiva o de nervio. Por lo tanto, exámenes mediante el uso de diapasones debe formar parte de todo examen físico en ambos niños y adultos.

Si sólo empleamos un diapasón, debemos elegir el de una frecuencia de 50 ciclos por segundo, ya que éste estaría menos influenciado por los ruidos usuales de la oficina o cuartos de exámenes que aquel de tono más bajo. Si empleamos un segundo diapasón debe ser el de 2,000 ciclos por segundo ya que esta es el área de frecuencia en la cual la pérdida neuro-sensorial es de mayor importancia en la percepción de la voz.

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Presentado en la Sexagésima Asamblea Anual de la Asociación Médica de Puerto Rico. San Juan, P. R., 13 de Noviembre de 1963.

**a. Prueba de Rinne:**

Establece la relación de percepción entre la vía aérea y la ósea, las dos vías de conducción del sonido.

Consiste en aplicar el diapasón vibrando sobre la apófisis mastoidea del lado que queremos explorar y cuando el enfermo deja de percibir el sonido, se sitúa por delante del conducto auditivo. Cuando el sonido se oye más por vía aérea que por vía ósea, se denomina Rinne positivo. Índice pérdida perceptiva.

Cuando el sonido se oye más por vía ósea que por vía aérea, se denomina Rinne negativo. Indica pérdida conductiva o de conducción.

**b. Prueba de Weber:**

Consiste en la comparación entre la conducción ósea de un lado y el opuesto. Colocando un diapasón vibrando sobre el vértex del cráneo el sonido se percibe normalmente con igual intensidad en ambos oídos. Cuando el sonido se percibe con más intensidad en el lado enfermo, indica alteración en el aparato de conducción del sonido, si por el contrario el sonido es percibido en el oído sano indica alteración del aparato de percepción.

**AUDIOMETRIA RADIOELECTRICA**

Registra en una ficha audiométrica la intensidad sonora en cada frecuencia. Nos da un perfil audiométrico óseo y aéreo con su adecuada interpretación.

**Audiogramas Típicos:**

1. Presbiacusia (sordera típica de la vejez)
2. Pérdida auditiva de tipo mixto (severa)
3. Pérdida auditiva de tipo mixto (moderada)
4. Sordera de conducción pura debido a otosclerosis no complicada.
5. Sordera perceptiva o neuro-sensorial (por afectación del nervio auditivo)

**BREVE REPASO DE LA FISIOLOGIA DE LA AUDICION**

**Las Vibraciones** de la platina del estribo producen movimiento del líquido perilinfático a lo largo de la escala vestibular y la escala timpánica. Dichas oscilaciones perilinfáticas son transmitidas através de las paredes del ducto coclear a el líquido endolinfático el cual a su vez estimula los receptores neuroepiteliales, que estimularán las vías auditivas hacia los centros de la audición

localizados en la primera y segunda circunvolución temporal, donde las impresiones se hacen conscientes.

#### ETIOLOGIA DE LAS SORDERAS INFANTILES

Pueden ser de tipo familiar o debido a un defecto en el desarrollo del embrión. Pueden ser causadas por daño intrauterino o al paso a través del canal del parto o a Eritroblastosis Fetal por incompatibilidad del factor Rh.

La sordera puede ser adquirida después del nacimiento y debida a variedad de causas entre las cuales están incluidas enfermedades tales como meningitis, enfermedades virásicas (particularmente sarampión o parotiditis), diabetes, sífilis, hiper-pirexia de tipo no específico y mixedema. Así como drogas ototóxicas como la Neomicina, Estreptomicina, Kanamicina, Salicilatos y Quinina, etc. Cada una de estas drogas puede afectar la cóclea y es conveniente advertir que debe descontinuarse cualquier droga que cause acúfenos ya que probablemente es el medio de expresión de afectación coclear temprana.

Otras causas de sordera tal como fracturas de cráneo, lesiones timpánicas secundarias a zambullidas y trauma acústico.

Sordera en casos de edad avanzada (Presbiacusia) comienza generalmente con frecuencias altas y progresiva igualmente la conducción aérea y ósea.

Ciertas condiciones del oído medio e interno pueden ser favorablemente resueltas mediante tratamiento médico o quirúrgico.

#### OTITIS MEDIA SEROSA

Generalmente sigue a una infección respiratoria tratada pron坦amente con antibióticos por lo cual los síntomas de dolor de oído, fiebre y supuración asociados comúnmente con otitis media, nunca aparecen. Una o dos semanas después la familia nota que hay que hablarle en tono de voz más alto al niño para conseguir su atención.

A la inspección el tímpano puede aparecer normal, pero en examen más detenido puede notarse ocasionalmente un nivel líquido o la presencia de burbujas en el líquido.

En caso de duda, se debe practicar una miringotomía diagnóstica en el cuadrante posterior inferior del tímpano seguido por aspiración del líquido.

Factores influyentes a episodios repetidos de otitis media serosa tal como tejido adenoideo hipertrófico, deben de ser eliminados. Cuando existe tendencia a reacumularse líquido, se puede colocar un pequeño tubo plástico (polietileno) por debajo del tímpano y dejarlo colocado por varios meses, no para que actúe como

tubo de drenaje, sino para que actúe como una trompa de Eustaquio accesoria, permitiendo la ventilación aérea del oído medio.

#### OTITIS MEDIA CRONICA

Se pueden subdividir en:

- Otitis media crónica simple
- Otitis media crónica adhesiva
- Otitis media crónica con colesteatoma

La otitis media crónica simple es el resultado final de una otitis media supurada aguda, la cual ha producido una perforación en la porción tensa del tímpano. Se debe tratar por todos los medios de secar el oído y una vez logrado esto, corregir el defecto del tímpano mediante un procedimiento quirúrgico denominado: miringoplastía (siempre y cuando exista continuidad de la cadena osicular).

La otitis media crónica adhesiva frecuentemente comienza por la otitis media serosa ya discutida. Si esta última no es tratada con éxito, el tímpano se retrae progresivamente por una presión negativa aparente en el oído medio. El problema parece recaer en una pérdida de función de la Trompa de Eustaquio. La parte postero-superior del tímpano o (pars flácida de Shrapnell) retraída por la presión negativa, tiende a formar bolsillos tapizados por epitelio escamoso (el comienzo de la complicación más temida de la otitis media adhesiva; el colesteatoma).

El colesteatoma es un tumor capsulado que contiene masas de colesterolina cuya membrana mucosa toma los caracteres de la piel; se inflama y degenera, provocando una expansión en la cual se produce erosión de los tejidos circundantes, incluyendo el hueso.

Algunas complicaciones del colesteatoma:

1. Parálisis facial por erosión de la pared ósea de la porción horizontal del nervio facial.
2. Meningitis
3. Laberintitis
4. Absceso epidural
5. Trombosis del seno lateral

#### Tratamiento:

Afortunadamente las técnicas micro-quirúrgicas desarrolladas bajo el Microscopio Operatorio proveen una oportunidad para remover material colesteatomatoso bajo visión directa magnificada con conservación e incluso aún mejoramiento de la función audi-

tiva. Mastoidectomía sin o con timpanoplastía subsiguiente es la operación indicada en este proceso colesteatomatoso.

#### ENFERMEDAD DE MENIERE

Esta causa importante de sordera (acúfenos-tinnitus) y vértigo en adultos es a menudo accesible a tratamiento médico o quirúrgico. Mediante etiología desconocida, la endolinfa se forma en cantidades excesivas, produciendo un aumento de presión a lo largo del ducto coclear y el sistema vestibular. Se puede detectar nistagmus, sólo en el momento del episodio típico de vértigo. Existe generalmente una pérdida auditiva neuro-sensorial.

#### Tratamiento:

Se han preconizado varios tipos de tratamiento médico, incluyendo el uso intravenoso de drogas como la Dramamina o antihistamínicos como la Piribenzamina o Benadryl. El uso de vasodilatadores del tipo del Acido Nicotínico; dieta libre de sal y diuréticos. Histamina intravenosa ha sido empleada con éxito en casos selectos. El uso de extractos adreno-corticales ha sido empleado recientemente. En casos refractarios incapacitantes, es necesario recurrir a laberintectomías quirúrgicas o a la destrucción selectiva del laberinto por ultrasonidos.

#### ACCIDENTES VASCULARES ACUSTICOS

Otro tipo de sordera que puede responder a tratamiento médico es la pérdida súbita de audición (usualmente unilateral); debida a espasmo vascular, o a un coágulo en uno de los vasos que suplen el oído interno.

Esta pérdida súbita de audición se acompaña generalmente de acúfenos y vértigo.

#### Tratamiento:

Hospitalización inmediata con heparinización, terapia de corticosteroides e histamina intravenosa suelen producir una mejoría dramática.

#### OTOSCLEROSIS

Esta es una de las causas más importantes de incapacidad auditiva en el adulto por;

1. Su incidencia relativamente alta en lo cual se estima un

4% de la población total, ó 35 ó 40% de aquellos incapacitados acústicamente.

2. El hecho de que es usualmente corregible, bien sea mediante una prótesis auricular (Hearing aid) o mediante los métodos modernos de micro-cirugía.

#### ANATOMIA PATOLOGICA DE LA OTOSCLEROSIS

Esta enfermedad es única a la cápsula ótica humana. Puede manifestarse en cualquier época de la vida, pero más frecuentemente después de la pubertad, durante el embarazo, puerperio o la menopausia. El proceso comienza por reabsorción de hueso en uno o más focos diminutos, los cuales se extienden gradualmente hasta coalescer. A veces, la cápsula entera está envuelta, incluyendo las paredes de los canales semicirculares y ambas ventanas laberínticas. El hueso reabsorbido es reemplazado por nuevo hueso colocado en diseños irregulares de tipo mosaico. No sólo se reemplaza el hueso normal por hueso esclerótico, sino que una pronunciada proliferación de hueso patológico se desarrolla y progresivamente oblitera la ventana oval. Mediante invasión de la platina del estribo, el hueso patológico immobiliza el 3er huesillo o estribo, de esta manera reduciendo la transmisión de vibraciones.

#### SINTOMAS

Normalmente comenzamos la vida con un grado mayor de audición del que necesitamos, y es solamente cuando nos acercamos a la pérdida auditiva de 30 decibelios, cuando notamos una disminución en la audición. Lo primero observado es la inabilidad para oír un murmullo o para entender la palabra hablada a distancia.

En las primeras etapas, la conducción ósea, mediante la cual oímos nuestras propias voces, permanece relativamente inafectada; por lo cual, para el otosclerótico, su propio tono de voz le parece extremadamente elevado. Para compensar, modula su tono de voz tan bajo hasta llegar casi a la inaudición. El otosclerótico oye mejor en reuniones de grupos los cuales todos alzan la voz para hablar, sobre el ruido circundante. Oyen bastante bien conversaciones telefónicas mediante conducción ósea inalterada.

#### TRATAMIENTO QUIRURGICO

La primera operación para mobilizar el estribo fijo fue practicada por el alemán Kessel<sup>1</sup> en 1878. Jenkins<sup>2</sup> en 1912, Barany<sup>3</sup>

en 1914 y Holmgren<sup>4</sup> en 1917 reanudaron operaciones en otoscleróticos. El francés Sourdille<sup>5</sup> en 1924 estableció mediante la timpano-laberintopexia la primera fenestración con éxito en un paciente con otosclerosis. Con algunas modificaciones técnicas, Lempert<sup>6</sup> en 1938 simplificó la técnica de Sourdille en una fenestración de una sola etapa.

En 1952, mediante una observación accidental, Rosen<sup>7</sup> revisó la abandonada operación, de mobilización del estribo.

En 1958 Shea<sup>8</sup> revivió la operación de estapediectomía preconizada por Blake<sup>9</sup> y Jack<sup>10</sup> en 1892, y añadió un injerto de vena y una prótesis de polietileno a la operación original.

#### Técnica del Dr. John Shea:<sup>11</sup>

Originalmente:

Vena del dorso de la mano y prótesis de polietileno.

Modificada últimamente por fenestra en la platina del estribo, con inserción de un pistón de acero inoxidable ó teflón, conectando el yunque con la platina del estribo fenestrada.

#### Técnica del Dr. Harold Schuknecht:<sup>12</sup>

Lazo de alambre con grasa del lóbulo de la oreja. El alambre cubre el proceso largo del yunque en su porción distal, y la grasa ocluye la ventana oval después de haber sido extraída la platina del estribo en su totalidad.

#### Técnica del Dr. Fred Guilford:<sup>13</sup>

Pistón de alambre teflón.

El alambre sobre la porción distal de el proceso largo del yunque, y la porción del Teflón, cubriendo la fenestra en la ventana oval.

Otolaringólogos prominentes como los doctores F. Antolí-Candela,<sup>14 15, 6</sup> de Madrid, España; F. Carnevale Ricci,<sup>17</sup> de Milán, Italia; M. Portmann,<sup>18</sup> de Bordeaux, Francia; H. Guillón,<sup>19</sup> de París, Francia, han contribuído a difundir sus técnicas personales y modificaciones de las ya mencionadas, en los países europeos, cuna original de la cirugía para corrección de las sorderas.

#### RESUMEN

De manera breve se presenta un repaso de la fisiología audi-

\* Descripción y nuevas modificaciones de la estapediectomía.

tiva, etiología de las sorderas y métodos de diagnóstico clínico y radioeléctrico de las mismas.

Técnicas en el Tratamiento Quirúrgico de la Otosclerosis han sido expuestas en resumen.

#### SUMMARY

Briefly a review of the physiology of hearing and etiology of deafness has been discussed.

Methods of clinical and radioelectric diagnosis of these are presented.

Techniques in the Surgical Treatment of Otosclerosis have been summarized.

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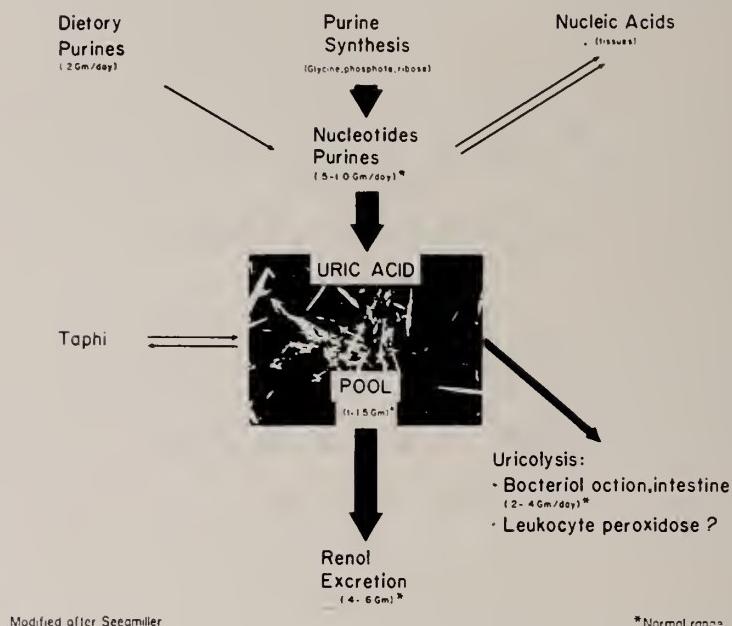
## EXHIBIT ON GOUT

JULIO V. RIVERA, M.D., F.A.C.P.

# PATHO-PHYSIOLOGY

A positive urate balance results from metabolic derangements.

### PURINE METABOLISM (HUMAN)



#### PRIMARY GOUT

- Hereditary disorder of purine metabolism
- Specific metabolic disturbance not yet identified: Increased endogenous purine synthesis demonstrable in 2/3 of the cases
- Excretion of uric acid not usually impaired

#### SECONDARY GOUT

- Caused by:
  - myeloproliferative diseases – polycythemia, myeloid metaplasia, leukemia, psoriasis
  - drugs – thiazides, pyrazinomide
- Increased nucleic acid synthesis
- In renal insufficiency hyperuricemia is frequent; gouty arthritis is rare.

FIG. 1

Exhibit entitled "Gout" presented at the 60th Annual Meeting of the Puerto Rico Medical Association. From the Veterans Administration Hospital, San Juan, P. R.



Fig. 2: Bilateral chronic olecranon bursitis in patient with gout.



Fig. 3: Knees showing suprapatellar effusion on the left one. No changes in bone or articular surfaces are seen. This is a frequent manifestation of gout.



Fig. 4: Tophus on the auricle, as shown here, occur in less than 10% of the cases.



Fig. 5: Section of tophus showing multicentric clusters of needle-like uric acid crystals arranged radially and surrounded by foreign-body granuloma(H-E).



Fig. 6: Large tophus adjacent to interphalangeal joint; smaller ones near metacarpophalangeal and carpal joints.



Fig. 7: Tophi on lateral aspect of foot and ankle.

Gout is a frequent cause of inflammatory arthritis in adult males. Recurrent inflammatory arthritis of rapid onset and short duration (4-14 days) is the usual presenting symptom. Involvement of lower extremity joints predominates. Clinical diagnosis should be established long before the advanced lesions pictured above occur.

# *MANAGEMENT*

A simple and effective therapeutic regime is available.

## ACUTE ARTHRITIS:

<i>Drug</i>	<i>Dose</i>	<i>Toxic Potential</i>
Colchicine, oral	0.5 mg/hour (8-15 doses)	Gastroenteritis
Colchicine, IV	1-2 mg/doy	
Phenylbutazone	0.2 Gm q 4 hours (4 doses); then 0.1Gm qid	Gl.edema, bone marrow depression

Aim is relief of acute inflammation

## INTERVAL:

<i>Drug</i>	<i>Dose</i>	<i>Toxic Potential</i>	<i>Cost *</i>
Colchicine	0.5 mg bid	Gastroenteritis	Lowest
Probenecid	1-3 Gm/day	Gastritis	Medium
Sulfinpyrozone	0.4-0.8 Gm/day	Bone marrow depression	Highest

Probenecid and sulfinpyrozone increase renal excretion of uric acid.  
 Aim is prevention of acute attacks, control of chronic joint changes  
 and dissolution of tophi. Treatment is continued indefinitely.

\* From Drug Topics Red Book, 1964

Julio V. Rivera, M. D. and M. Martinez-Maldonado, M. D.  
*Medical and Radiological Services*

R. Bernabe-Prida, B. S. Ph., *lettering*  
 J. Muntaner, *photography*

*The cooperation of the X-ray and Pathology Services  
 and Engineering Division is acknowledged.*

# AN OUTBREAK OF DIARRHEA AT THE SAN JUAN CITY HOSPITAL DEPARTMENT OF PEDIATRICS

AIDA GUARDIOLA-ROTEGER, M.S., Ph.D.\*

VICTOR A. LOPEZ, M.D.

## INTRODUCTION

The occurrence of sporadic cases and hospital nursery epidemics as well as extensive community outbreaks of diarrhea associated with enteropathogenic **Escherichia coli** 0111:B4 has been previously described in the literature.<sup>1-5</sup> This report includes data on the prevalence of enteropathogenic **E. coli** 0111:B4 at the Pediatric Ward of the San Juan City Hospital during the calendar year 1963, as well as an outbreak which occurred during the months of August and September of that year.

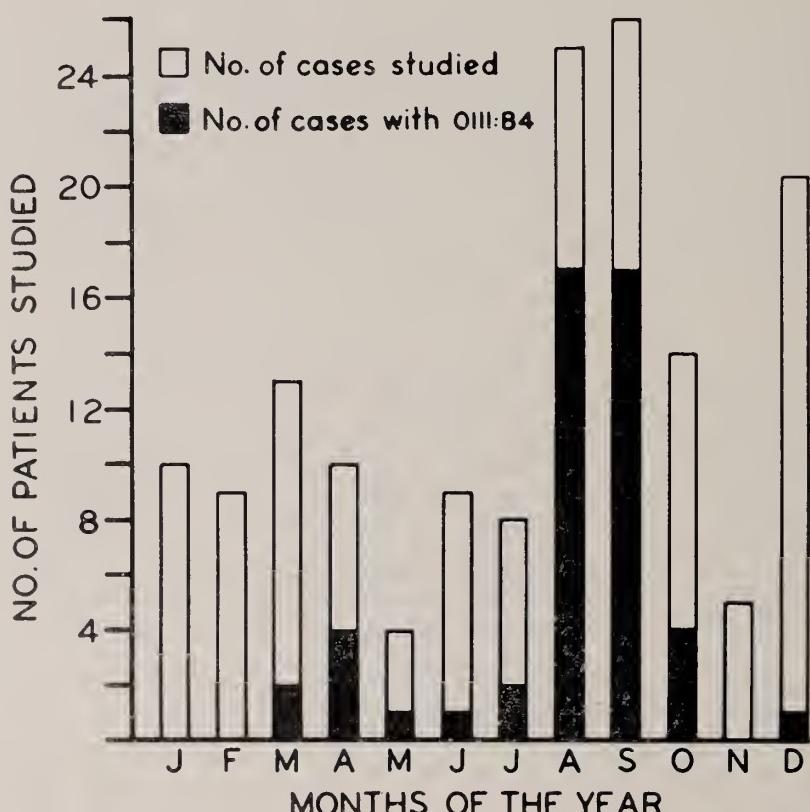
With the assistance of the attending personnel of the Department of Pediatrics, San Juan City Hospital, a survey for enteropathogenic **E. coli** 0111:B4 was undertaken. During the course of the studies on diarrheal diseases of infancy which are being conducted at the above mentioned hospital, the prevalence of enteropathogenic **E. coli** 0111:B4 was noticeable. The monthly distribution of this serotype during the calendar year of 1963 is shown in Figure 1. This survey was prompted when one of the patients under study, showed what seemed at that time a hospital acquired infection with 0111:B4. This girl had shown negative stool cultures for three consecutive days after admission, and on the fifth day gave a one hundred percent (100%) stool culture of 0111:B4. On August, 28, all children in the Diarrhea Ward were studied to determine the incidence of this serotype and new admissions from this date through September 30, were included in the survey. The survey was repeated during the second, third and fourth days of December.

## MATERIALS AND METHODS

A swab, either rectal or dipped in freshly passed stool, was obtained from each child and immediately placed in 1 ml of saline. After incubation at room temperature for 2 hours, smears were prepared from the saline suspension, fixed by heat, and stained for 30 minutes at room temperature with commercial (Difco) fluorescein isothiocyanate conjugated **E. coli** immune globulin, washed twice in buffered saline and distilled water and then dried at room temperature. The mounted smear was examined with a Leitz

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**FIGURE I**  
**MONTHLY DISTRIBUTION OF *E. COLI* OIII:B4 IN  
 THE DIARRHEA WARD, DEPT. OF PEDIATRICS,  
 SAN JUAN CITY HOSPITAL DURING 1963.**



fluorescence microscope with a BG-12 (blue-pass) exciter filter and a blue absorption secondary filter.

The fecal suspension was further incubated overnight at room temperature and then streaked on a MacConkey agar plate. The isolated enteropathogenic *E. coli* were characterized biochemically, and typed according to the methods described by Edwards and Ewing.<sup>6</sup>

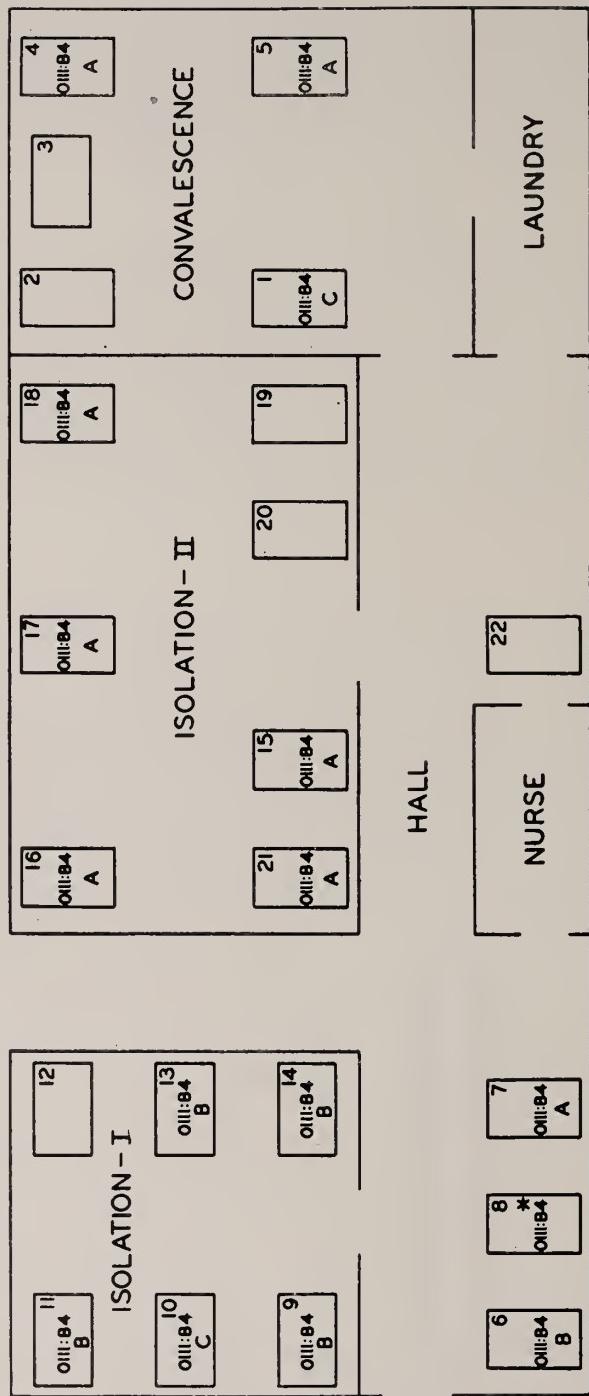
Stool samples and throat saline gargles were obtained from most of the personnel who were in either direct or indirect contact with the patients. Their stool samples were processed in a similar manner to that followed with the patient's samples. The nasopharyngeal washings obtained were shaken in tubes with the aid of glass beads, the suspension obtained was centrifuged for 10 minutes at 2000 RPM and the supernate removed by decanting. The sediment was then processed as previously described for the stool samples.

## RESULTS

A survey for enteropathogenic *E. coli* O111:B4 was conducted in 22 children with gastroenteritis hospitalized at the San Juan City Hospital on August 28, 1963. The clinical records revealed that all but one had negative stool cultures for this organism on admission. However, on the survey day, a total of 15 (68.1%) gave positive stool cultures for O111:B4, and in 16 cases (72.7%) this serotype was also detected by immunofluorescence as shown in Table 1. The epidemiological characterization of the O111:B4 serotype isolated from 15 patients was performed. The biochemical reactions given by the cultures conformed to those described by Edwards and Ewing.<sup>6</sup> The antibiotic sensitivity patterns data obtained with polymyxin, chloromycetin, erythromycin, kanamycin, novobiocin, penicillin, streptomycin, tetracycline, terramycin, neomycin and furoxone are shown in Table 2. All of the 15 cultures obtained were moderately susceptible to polymyxin. Eight (53.3%) of them were susceptible only to polymyxin; 5 (23.3%) cultures were also moderately susceptible to chloromycetin and terramycin, and the remaining 2 cultures (13.3%) were also susceptible to furoxone. As it can be seen from Table 2, none of the patients were treated prior to the stool collection with the given effective antibiotic.

The patient's distribution in the Diarrhea Ward on August 28 is shown in Figure 2. The *E. coli* O111:B4 was present in both isolation cubicles as well as in the convalescence room. The patients with strains sensitive only to polymyxin (Group A) were mainly located in the Isolation II room, whereas the patients belonging

**FIGURE II**  
**LOCATION OF PATIENTS IN THE DIARRHEA WARD**  
**AUGUST 28, 1963**



A } ANTIBIOTIC SENSITIVITY  
 B } ACCORDING TO TABLE 2  
 C }  
 OII:B4\* DETECTED BY IMMUNOFLUORESCENCE ONLY

to the Group B sensitivity range were located in Isolation I room.

Stool samples were obtained from these patients one and two weeks after initial collection. The results obtained are shown in Table 1. The number of patients with positive stool cultures decreased (13.3%) in the first week. In the second week no positive cultures were obtained as expected, since controlled antibiotic therapy had been initiated. However, the 0111:B4 was still detected by immunofluorescence in 60% of the patients. This can well be explained by the fact that the patients had been treated with antibiotics and thus rendered negative stool cultures. Similar results have been reported in the literature.<sup>4</sup>

The attending personnel at the department of pediatrics were also studied. A total of 53 gargle samples and 16 stool specimens were obtained and studied for the presence of enteropathogenic *E. coli* by immunofluorescence. One case (6.6%) had 0111:B4, 4 (26.5%) had 026:B6 and 3 (20.0%) had 0124:B17 in the stool samples. For the gargle samples, 15 (28.3%) yielded 0111:B4, 11 (20.7%) had 026:B6 and 1 (1.8%) had 0124:B17. In addition to being detected by immunofluorescence the O111:B4 serotype was isolated from the gargle washings of one of the nurses and the culture was found to belong to the Group A sensitivity pattern shown in Table 2. The relationship of these findings to the hospital outbreak can not be stated with certainty since there are not enough data of statistical significance. The possible respiratory transmission of enteropathogenic *E. coli* 0126:B16 during epidemics by pharyngeal carriers has been discussed by some investigators.<sup>7</sup>

All children admitted to the Diarrhea Ward during the period following 28 August 1963 thru 30 September 1963 were also included in the survey. The results are shown in Table 3.

A total of 25 children were admitted and studied during this period. On admission 1 child (4.0%) had O111:B4 and 3 (12.0%) had enteropathogenic *E. coli* which were not identified as to serotype. On the week following admission 9 (36.0%) were positive for 0111:B4 by culture and FA and this serotype was detected by immunofluorescence only in another 9 (36.0%) children. In the second week after admission 21 of the 25 children were still hospitalized. Of these, 7 (33.3%) were positive by both methods and in addition, 4 (17.0%) yielded 0111:B4 by immunofluorescence only. In the third week, 16 children remained in the hospital and 8 (50.0%) were positive by cultures and FA, in 7 (43.6%) additional cases the serotype was detected by immunofluorescent techniques only. These data show that although the outbreak had been controlled to a certain extent, children with negative stool cultures for 0111:B4 on admission still became positive cases

TABLE 1

Survey for enteropathogenic *E. coli* 0111:B4 at the Pediatric Ward,  
San Juan City Hospital on 28 August 1963.

Patient Number	EPEC data prior to 28 Aug. 63	Antibiotic therapy on admission prior to stool collection	0111:B4 in stool specimen				
			28 Aug. 63 C*	3 Sept. 63 FA**	10 Sept. 63 C	FA	
17	6-9 Aug. (-) 14 Aug. (+)	Kaomycin, Penicillin Terramycin, Kanamycin	+	+	-	+	Discharged
6	22 Aug. (-)	None	-	+	Died		
9	24-26 Aug. (-)	None	+	+	-	+	- -
18	6-9-14 Aug. (-)	Furoxone, Chloromycetin, Kaomycin	+	+	-	+	Discharged
10	6-14 Aug. (-)	Kanamycin, Penicillin	+	+	Died		
1	26 Aug. (-)	None	+	+	Discharged		
13	10 Aug. (-)	Kaomycin	+	+	-	-	- -
5	14 Aug. (-) 30 Aug. (-)	Penicillin, Kaomycin	+	+	-	+	- +
14	25-26 Aug. (-) 27 Aug. (+)	Kaomycin, Colimycin	+	+	-	-	Discharged
7	Unknown	Penicillin, Kaomycin	+	+	-	+	Discharged
15	30 July (-) 27 Aug. (+)	Penicillin, Kaomycin	+	+	-	-	Discharged
16	20-22 Aug. (-)	Kaomycin	+	+	-	+	- -
11	14-19-27 Aug. (-)	Kaomycin	+	+	-	+	Discharged
4	8 Aug. (-) 14-15 Aug. (+)	Kaomycin	+	+	Discharged		
21	21 Aug. (-)	None	+	+	+	+	+
8	26 Aug. (-)	Kaomycin	-	+	+	+	- +
19	12 Aug. (-) 13 Aug. EPEC	Furoxone Kaomycin	-	-	Discharged		
2	9-12 (-) 13 (+)	Chloromycetin	-	-	Discharged		
12	23 Aug. (-) 26 Aug. (+)	Kaomycin Colimycin	-	-	-	-	Discharged
20	10 Aug. (-) 12 Aug. (+)	Furoxone, Chloromycetin Kaomycin	-	-	-	-	Discharged
22	27 Aug. (-)	None	-	-	Died		
3	18 July (-) 2-15 Aug. (+)	Chloromycetin, Furoxone	-	-	Discharged		

Total Studied (28 Aug. 63) — 22

Positive EPEC on Admission — 0

Positive Culture 0111:B4 (28 Aug.) — 15 (68.1%)

Positive FA 0111:B4 — (28 Aug.) — 16 (72.7%)

C\* — culture

FA\*\* — fluorescent antibody techniques

during the first, second and even third week after admission. The antibiotic sensitivity patterns of the strains isolated are shown in Table 4. Nine of the patients (56.2%) had 0111:B4 highly sensitive to chloromycetin, terramycin and tetracycline and moderately sensitive to furoxone (Group D). In five cases (31.2%) the organism was found to be moderately sensitive to furoxone and polymyxin (Group C) and one each (4.5%) were sensitive to polymyxin (Group A) and chloromycetin and polymixin (Group E). The majority belonged to Group D, which differed from the sensitivity patterns shown in Table 2, since the strains were re-

TABLE 2

Antibiotic Sensitivity Patterns of the *E. coli* 0111:B4 isolated from the San Juan City Hospital Pediatric Cases on August 28, 1963.

Culture Isolated from Patient No.	Susceptibility		Antibiotic therapy on Admission prior to stool Collection
	High	Moderate	
4		Polymyxin	Kaomycin
5		Polymyxin	Penicillin Kaomycin
7		Polymyxin	Penicillin Kaomycin
15		Polymyxin	A Penicillin Kaomycin
16		Polymyxin	Kaomycin
17		Polymyxin	Kaomycin, Penicillin Terramycin
18		Polymyxin	Furoxone, Chloromycetin Kaomycin
21		Polymyxin	None
9	Chloromycetin Terramycin	Polymyxin Tetracycline	B None
11	Chloromycetin Terramycin	Polymyxin Tetracycline	Kaomycin
13	Chloromycetin Terramycin	Polymyxin Tetracycline	Kaomycin
14	Chloromycetin Terramycin	Polymyxin Tetracycline	Kaomycin Colimycin
6	Chloromycetin Terramycin	Polymyxin Tetracycline	Kaomycin
1	Furoxone	Polymyxin	C None
10		Polymyxin Furoxone	Kaomycin, Penicillin Chloromycetin

sistant to polymyxin and sensitive to furoxone in contrast to Groups B of Table 2.

The survey for enteropathogenic *E. coli* 0111:B4 was repeated during the month of December, this time Wards A, B and D where patients are admitted for illnesses other than gastroenteritis were included in addition to Ward C, the Diarrhea Ward. Two swabs, either rectal or dipped in freshly passed stools were collected from each patient. One was emulsified in saline and the second one in trypticase soy broth. The suspensions were then in-

TABLE 3

Survey for Enteropathogenic *E. coli* 0111:B4 on new admissions after  
28 August 1963 thru 30 September 1963 at the Pediatric Ward,  
San Juan City Hospital

Patient No.	Admission Date	0111:B4 in Stool Culture			
		On Admission	1st week	2nd week	
6B	30 Aug. 63	Neg	Pos	Neg	Pos*
7B	31 Aug. 63	Neg	Pos*	Died	
10B	31 Aug. 63	Neg	Pos*	Disch.	
44B	2 Sept. 63	EPEC**	Pos	Neg	Not Done
19B	2 Sept. 63	EPEC**	Neg	Neg	Pos*
8C	3 Sept. 63	EPEC**	Pos*	Pos*	Disch.
20C	4 Sept. 63	Neg	Neg	Neg	
18C	5 Sept. 63	Pos	Pos	Pos	
8D	8 Sept. 63	Neg	Pos	Neg	Pos*
17D	8 Sept. 63	Neg	Pos	Pos	Pos
19D	9 Sept. 63	Neg	Pos*	Pos	Neg
13D	10 Sept. 63	Neg	Neg	Neg	Pos*
14D	10 Sept. 63	Neg	Pos*	Disch.	
4D	11 Sept. 63	Neg	Pos*	Neg	Pos*
10D	12 Sept. 63	Neg	Pos	Neg	Pos
21E	13 Sept. 63	Neg	Pos	Pos	Neg
7E	14 Sept. 63	Neg.	Pos*	Pos*	Pos
11E	14 Sept. 63	Neg	Pos*	Neg	Pos*
16E	14 Sept. 63	Neg	Pos	Pos	Pos*
18E	15 Sept. 63	Neg	Pos	Disch.	
22E	17 Sept. 63	Neg	Neg	Pos	Pos
15E	17 Sept. 63	Neg	Neg	Pos	Pos
22F	18 Sept. 63	Neg	Neg	Pos*	Pos
2E	19 Sept. 63	Neg	Neg	Neg	Pos
8E	19 Sept. 63	Neg	Pos*	Pos*	Pos

Pos\* — positive for 0111:B4 by immunofluorescence only.

EPEC\*\* — isolate not typed.

TABLE 4

Antibiotic Sensitivity Patterns of the *E. coli* 0111:B4 isolated from the San Juan City Hospital from 30 August thru 30 September 1963

Culture Isolated from Pt. No.	Susceptibility		Antibiotic therapy prior to stool collection
	High	Moderate	
4B		Polymyxin	Kaomycin
8D		Furoxone Polymyxin	A Kaomycin, Cloromycetin
10D		Furoxone Polymyxin	Kaomycin
7E		Furoxone Polymyxin	Kaomycin
21E		Furoxone Polymyxin	Kaomycin
15E		Furoxone Polymyxin	Kanamycin, Kaomycin
18C	Chloromycetin Terramycin Tetracycline	Furoxone	Kaomycin
17D	Chloromycetin Terramycin Tetracycline	Furoxone	C Kaomycin
19D	Chloromycetin Terramycin Tetracycline	Furoxone	Kaomycin
16E	Chloromycetin Terramycin Tetracycline	Furoxone	Kaomycin
18E	Chloromycetin Terramycin Tetracycline	Furoxone	Kaomycin
22E	Chloromycetin Terramycin Tetracycline	Furoxone	Kaomycin
2E	Chloromycetin Terramycin Tetracycline	Furoxone	D Kaomycin Kanamycin
8E	Chloromycetin Terramycin Tetracycline	Furoxone	Kaomycin
22F	Chloromycetin Terramycin Tetracycline	Furoxone	Kaomycin
6B	Chloromycetin	Polymyxin	E Kaomycin

cubated at room temperature for 2 hours. Immunofluorescence studies were carried out on the saline suspension as previously described. The suspensions were further incubated overnight at room temperature, and then inoculated into bacterial culture media as described before. A total of 65 patients were studied. Only 20 of these cases had been admitted to the Diarrhea Ward with gastroenteritis as the clinical diagnosis. The data obtained are shown in Table 5. In the Diarrhea Ward (C) no 0111:B4 was isolated, and in only 2 cases (10.0%) this serotype was detected by immunofluorescence. In Ward D, the serotype was neither isolated nor detected; the organism was detected only in one patient (5.5%) from Ward B; and in Ward A it was detected and isolated in one case (5.0%). Although the incidence of *E. coli* 0111:B4 had subsided, the 0119:B14 serotype was prevalent in the Diarrhea Ward 30.0% isolated and 35.0% detected by immunofluorescence. This serotype was prevalent also in the remaining

TABLE 5

Enteropathogenic *E. coli* recovered at the Pediatric Department, San Juan City Hospital during the survey conducted in December 1963.

Ward		A	B	C*	D
Date of survey		4 Dec. 63	3 Dec. 63	2 Dec. 63	2 Dec. 63
No.	Patients Studied	20	18	20	7
0111:B4	Culture	No.	1	0	0
		%	5.0	0	0
	FA**	No.	1	1	2
		%	5.0	5.5	10.0
0119:B14	Culture	No.	2	9	6
		%	10.0	50.0	30.0
	FA	No.	15	15	7
		%	75.0	83.3	35.0
0124:B17	Culture	No.	0	0	0
		%	0	0	0
	FA	No.	0	0	3
		%	0	0	15.0
Others (0125:B15, 026:B6 0128:B12, 055:B5)	Culture	No.	1	0	0
		%	5.0	0	0
	FA	No.	3	0	1
		%	15.0	0	5.0

C\* — Diarrhea Ward

FA\*\* — Immunofluorescent techniques

three Wards: Ward A, 10.0% isolated, 75.0% detected; Ward B, 50.0% isolated, 83.3% detected; and in Ward D the serotype was detected only in 42.8% of the cases. The sensitivity patterns to streptomycin, penicillin, erythromycin, tetracycline, novobiocin, polycillin, furoxone, chloromycetin, colymycin, neomycin and kanamycin, showed that all the isolated strains were highly susceptible to furoxone and moderately susceptible to chloromycetin. These data point out the possibility of another hospital epidemic, unfortunately no data on admission cultures are available to make an accurate evaluation of the problem.

#### DISCUSSION

Three surveys for *E. coli* 0111:B4 were conducted at the Department of Pediatrics, San Juan City Hospital.

It seems obvious from the laboratory data presented that an outbreak due to *E. coli* 0111:B4 occurred at the Diarrhea Ward during the latter part of August thru September 1963. The laboratory findings on admission and the results obtained after the patients had been in the hospital anywhere from 3 days to 3 weeks point out to the possibility of a hospital acquired infection. The epidemiological characterization and antibiotic sensitivity patterns showed that the 0111:B14 serotype was evenly distributed in the ward. The marked antibiotic resistance of the strains isolated during the outbreak was noted. The resistance of the latter strain to neomycin is especially noteworthy since this antibiotic was the drug of choice at this hospital.

The data obtained from the nasopharyngeal washings of the attending personnel raised the question of the importance of possible respiratory transmission of enteropathogenic *E. coli* serotypes during epidemics.

The data obtained during the second survey conducted in December 1963 showed that the 0111:B4 outbreak was already in a progressively declining slope of the epidemiologic curve. However, the high incidence of the 0119:B4 serotype was startling. This serotype was found in the Diarrhea Ward, as well as in the remaining 3 wards where the patients are admitted for illnesses other than gastroenteritis. The epidemiological characterization and sensitivity patterns of the strains isolated from the Diarrhea Ward were similar to those obtained for the strains isolated from the remaining wards. Unfortunately the laboratory findings on admission are incomplete and follow-ups were not carried out, therefore a statistical evaluation of the problem can not be made.

The fluorescent antibody methods yielded more positive findings than the conventional culture methods. This observation was especially made in cases where the patients had been treated with

antibiotics prior to stool collection. It seems that the bacteria which had been inhibited or killed by antibiotics, failed to grow on bacteriologic media but would be detected by immunofluorescence. In some instances, no antibiotic treatment had been given, and yet the organism was detected only by immunofluorescence. It appears that persons probably harboring fewer organisms would yield positive findings by FA only. These could well be carriers or asymptomatic cases treated with antibiotics for long periods of time and which could well be missed in routine bacteriological studies. Nevertheless they are potential sources for spreading the organism and thus initiate an epidemic if proper control measures are not taken.

#### SUMMARY

1. Two surveys for *E. coli* 0111:B4 were conducted at the Department of Pediatrics of the San Juan City Hospital.
2. On August 28, 1963, 22 children in the Diarrhea Ward were studied as well as 63 nasopharyngeal washings and 15 stool specimens collected from the attending personnel. All children (25) admitted to this Ward following August 28 thru September 30, 1963 were also included in the studies.
3. A second survey was conducted during the month of December in all four wards of the Department of Pediatrics. A total of 65 children were then studied.
4. The laboratory data obtained showed that an outbreak due to *E. coli* 0111:B4 occurred at the Diarrhea Ward during the latter part of August thru September 30, 1963. The isolated strains had a marked resistance to antibiotics and especially to neomycin, the choice drug at the hospital. Three sensitivity patterns were obtained for the isolated strains.
5. The possible respiratory transmission of *E. coli* serotypes infections is discussed.
6. On the second survey, December 1963, the 0111:B4 outbreak was in the declining slope of the epidemiologic curve.
7. A possible 0119:B14 outbreak was observed in all four wards of the Department of Pediatrics during December 1963.
8. Fluorescent antibody methods yielded more positive findings than conventional culture methods. This was especially noted in persons undergoing antibiotic treatment.

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#### RESUMEN

1. Dos estudios sobre la incidencia de *E. coli* 0111:B4 se llevaron a cabo en el Departamento de Pediatría, Hospital de la Ciudad de San Juan.

2. El 28 de agosto de 1963, se estudiaron las heces de 22 niños de la sala de diarrea así, como 63 gárgaras y 15 muestras fecales obtenidas del personal encargado. Los 25 niños admitidos a esta sala entre el 28 de agosto y el 30 de septiembre de 1963 fueron también objeto de este estudio.

3. El segundo estudio se llevó a cabo durante el mes de diciembre incluyéndose esta vez las cuatro salas que comprenden el Departamento de Pediatría. Un total de 65 niños fueron estudiados en esta ocasión.

4. Los datos obtenidos demostraron que ocurrió un brote de *E. coli* 0111:B4 en la sala de diarrea durante los últimos días del mes de agosto y todo el mes de septiembre de 1963. Las cepas aisladas demostraron una tenaz resistencia a los antibióticos probados y especialmente a la Neomycina, esta última la preferida del hospital en este caso. Se obtuvieron tres grupos distintos de susceptibilidad entre las cepas aisladas.

5. La posibilidad de transmisión respiratoria de las infecciones intestinales de *E. coli* es discutida.

6. En el segundo estudio, diciembre de 1963, se demostró que la incidencia de *E. coli* 0111:B4 se encontraba en el segmento descendente de la Curva epidemiológica.

7. Un posible brote de *E. coli* 0119:B14 se descubrió en el Departamento de Pediatría en el mes de diciembre de 1963.

8. Las pruebas de immunofluorescencia demostraron más casos positivos que los métodos convencionales de cultivo. Esta diferencia fue más marcada en los casos que estaban bajo tratamiento con antibióticos.

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**RADIODIAGNOSIS**  
*HERIBERTO PAGAN SAEZ, M.D.*

**Case Summary (No. 6-63):**

This 26 year-old white male is approximately three feet tall. His extremities are extremely short and thick and his feet are deformed. The patient's sister has a similar condition.

Alkaline phosphatase: normal.



Fig. 6

\* From the Department of Radiology, School of Medicine, School of Tropical Medicine, University of Puerto Rico, Rio Piedras, Puerto Rico.

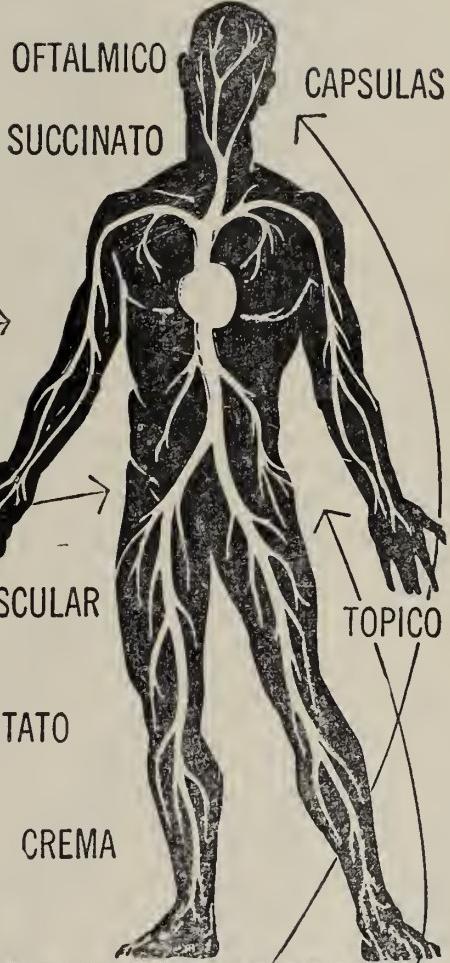
**Interpretation:**

There is marked shortening of the visualized long bones. The metaphyses show splaying associated with increased thickness of the corticalis and prominent epiphyses tuberosities.

**Diagnosis:**

Achondroplasia is defined as an hereditary and congenital growth disturbance of enchondral bone formation associated with dwarfism which exhibits retardation and irregularity of the growth of the cartilage of the epiphyseal ends of the bones. The circumferential bone formation is ordinarily less hindered.

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### **Section 1**

**T**HE PRINCIPAL objective of the medical profession is to render service to humanity with full respect for the dignity of man. Physicians should merit the confidence of patients entrusted to their care, rendering to each a full measure of service and devotion.

#### **1. CHARACTER OF THE PHYSICIAN**

The prime object of the medical profession is to render a service to humanity; reward or financial gain is a subordinate consideration. Whoever chooses this profession assumes the obligation to conduct himself in accord with its ideals. A physician should be "an upright man, instructed in the art of healing." He must keep himself pure in character and be diligent and conscientious in caring for the sick. As was said by Hippocrates, "He should also be modest, sober, patient, prompt to do this whole duty without anxiety; pious without going so far as superstition, conducting himself with propriety in his profession and in all the actions of his life." (*Principles of Medical Ethics, 1955 edition, Chapter I, Section 1.*)

#### **2. ABILITY OF PATIENT TO PAY**

One of the strongest holds of the profession on public approbation and support has been the age-old professional ideal of medical service to all, whether able to pay or not. That ideal is basic in our ethics. The abandonment of that ideal and the adoption of a principle of service only when paid for would be the greatest step toward socialized medicine which the medical profession could take. All our arguments as to better service to the people, freedom of choice of doctors would be as naught if such service were not available to a vast proportion of the people. (*House of Delegates, 1934*)

#### **3. FREE CHOICE OF PHYSICIAN**

Free choice of physician is defined as that degree of freedom in choosing a physician which can be exercised under usual conditions of employment between patients and physicians. The interjection of a third party who has a valid interest, or who intervenes between the physician and the patient does not *per se* cause a contract to be unethical. A third party was a valid interest when, by law or volition, the third party assumes legal responsibility and provides for the cost of medical care and indemnity for occupational disability. (*Principles of Medical Ethics, 1955 edition, Chapter VII, Section 4.*)

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Mellaril (thioridazine) relieves such anxiety, helping the patient to deal competently with the stresses of everyday life. Non-habituating, it can be given for extended periods of time. It does not “separate” the patient from practical problems and pressures, does not induce euphoria or a fuzziness which can compromise the ability to cope with realities. Rather, it helps the patient move more competently in his daily world by eliminating useless tension, by allowing him to conserve emotional resources and energies, and to direct them against the problems really worth worrying about. When efficacy is thus combined with a remarkable minimum of side effects, the physician is indeed

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*Contraindications:* Any severely depressed or comatose state.





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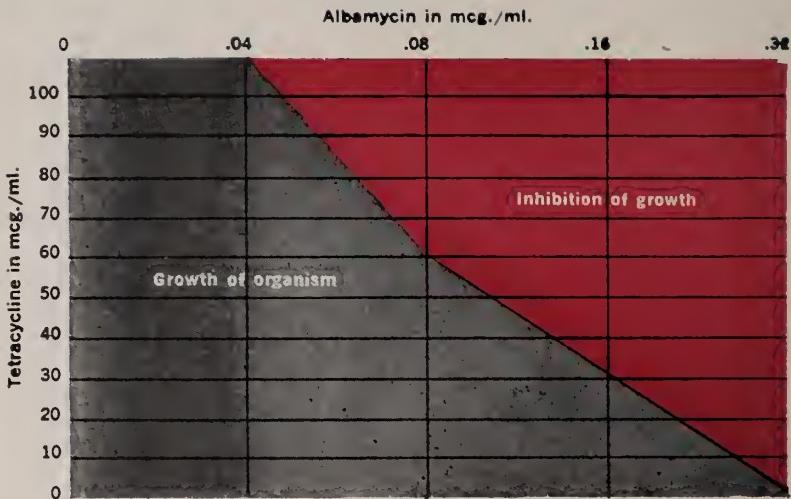
**DOSAGE:** Adults: In severe iron-deficiency anemia, 2 capsules or 1 tablespoonful 3 times daily after meals. As dietary supplement, 1 capsule or 1 tablespoonful morning or night. Children: 1 or 2 teaspoonsfuls, according to age.

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# Boletín *de la* Asociación Médica de Puerto Rico

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VOL. 56

JUNIO, 1964

NO. 6

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ENTERED AS SECOND CLASS MATTER, JANUARY 21, 1931 AT THE POST OFFICE AT SAN JUAN,  
PUERTO RICO UNDER THE ACT OF AUGUST 24, 1912.

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# BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO

Fundado en el 1903 y publicado mensualmente en San Juan, Puerto Rico

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El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudieran ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor se solicita de los autores que sigan las siguientes instrucciones:

a) Los trabajos deberán estar escritos a máquina a doble espacio y por un solo lado de cada página, en duplicado y con amplio margen.

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c) Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: (1) introducción, (2) material y métodos, (3) resultados, (4) discusión, (5) resumen (en español e inglés), (6) referencias.

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f) Si un artículo ha sido leído en alguna reunión o conferencia debe así hacerse constar.

g) Deben usarse los nombres genéricos de los medicamentos. Pueden usarse también los nombres comerciales, entre paréntesis, si así se desea.

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i) Las fotografías y microfotografías se someterán como copias en papel de lustre sin montar. Los dibujos y gráficas deben prepararse a tinta negra y en papel blanco. Todas las ilustraciones deben estar numeradas (números arábigos) e indicar la parte superior de las mismas. Debe escribirse una leyenda para cada ilustración e indicarse en el texto donde debe ir colocada. Un máximo de 6 ilustraciones, por artículo, serán permitidas sin costo para el autor.

j) Las referencias deben ser numeradas sucesivamente de acuerdo con su aparición en el texto. Los siguientes ejemplos pueden servir de modelo:

6. Koppisch, E. Pathology of arteriosclerosis. Bol. Asoc. Med. P. Rico 46: 505, 1954. (artículo de revista)
4. Wintrobe, M. M. Clinical Hematology, 3rd Ed. Lea and Febiger, Philadelphia, 1952, p. 67. (libro)

Deben usarse solamente las abreviaturas indicadas en el Index Medicus, Biblioteca Nacional de Medicina.

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In order to facilitate review of the article by the Editorial Board and the preparation of the manuscripts for the printer the authors are requested to follow the following instructions:

a) The entire manuscript, including figure legends and references, should be typewritten double-spaced in duplicate with ample margins.

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c) Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: (1) introduction, (2) material and methods, (3) results, (4) discussion, (5) summary in English and Spanish, (6) references.

d) Case reports will include (1) introduction, (2) description of the case, (3) discussion, (4) summary in English and Spanish and (5) references.

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g) Generic names of drugs should be used. Trade names may also be given in parenthesis if desired.

h) Metric units of measurements should be used preferentially. Abbreviations should be used sparingly.

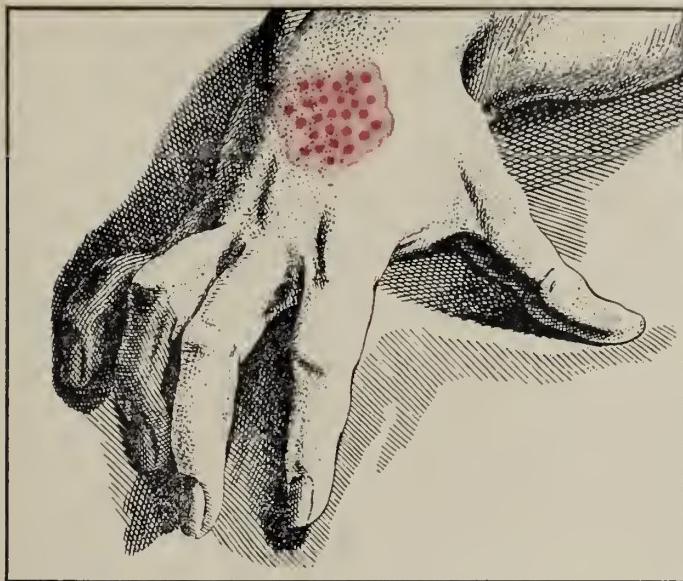
i) Photographs and photomicrographs should be submitted as glossy prints, unmounted. Drawings and graphs should be made in black ink on white paper. All illustrations should be numbered (Arabic) and top indicated. A legend should be given for each and its location should be indicated in the text. A maximum of 6 illustrations is allowed without cost to the authors.

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For complete product details, consult Schering literature available from your Schering representative, or Medical Services Department, Schering Corporation, Union, New Jersey.

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**References:** 1. Peele, J. C.: Med. Times 86:1228 (Oct.) 1958. 2. Riddle, A. C., Jr.: Oral Surg., Oral Med., Oral Pathol. 8:617 (June) 1955. 3. Lamphier, T. A.: Clin. Med. (Dec.) 1962.

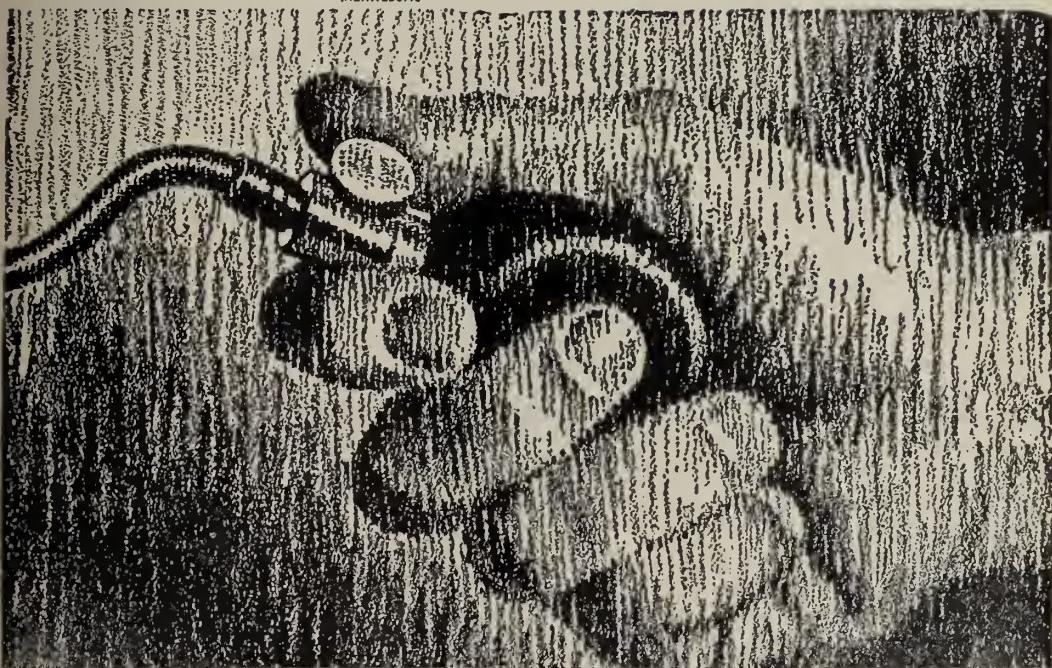
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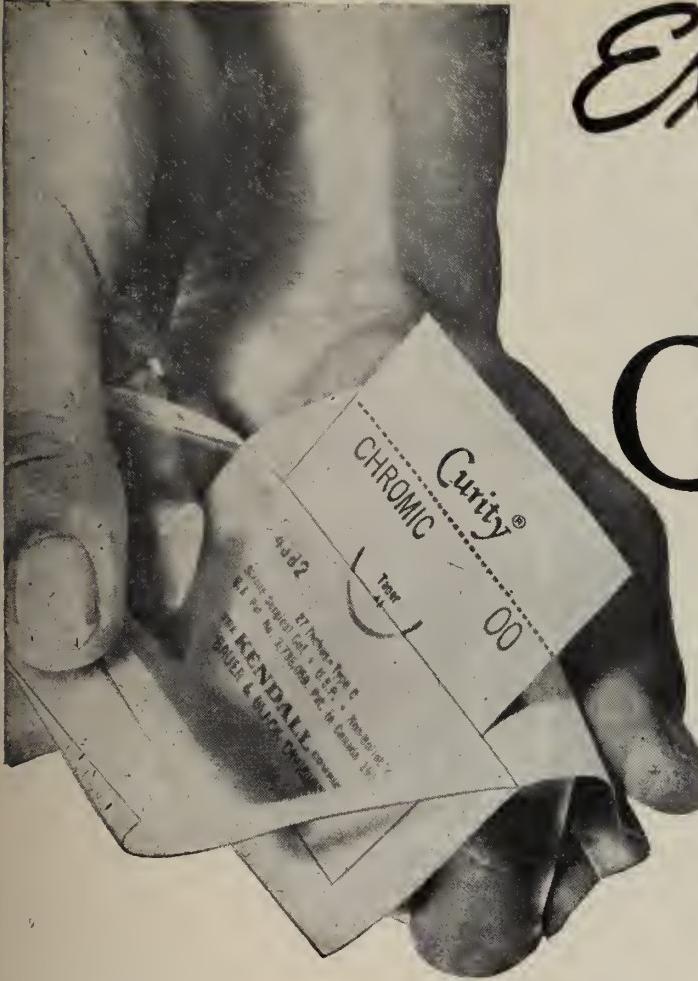
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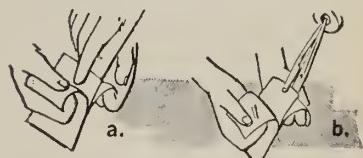
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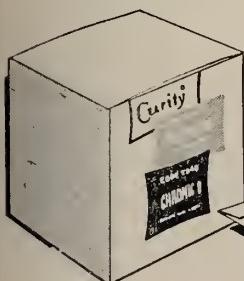
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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



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**Precautions:** Anuria.

\*From clinical data on file at Lederle Laboratories. Posed by model.

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# BOLETIN

DE LA ASOCIACION MEDICA DE PUERTO RICO

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## DREPANOCITEMIA-TALASEMIA

INFORME DE PRIMEROS CASOS EN PUERTO RICO

GERVASIO PRADO, M.D.; JOSE O. SANTANA, M.D.; y  
HECTOR F. RODRIGUEZ, M.D.\*

La incidencia en Puerto Rico de las hemoglobinopatías y en particular de la drepanocitosis ha sido objeto de varias comunicaciones. Pons y Oms,<sup>1</sup> en 1934, utilizaron la técnica del fenómeno drepanocítico provocado con un resultado positivo en el 5.6% de los individuos estudiados. En 1957 Torregrosa y colaboradores<sup>2</sup> encontraron que la incidencia de drepanocitosis en una serie de 818 puertorriqueños fué de 4.2% y de 6.7% cuando solamente se consideró individuos de la raza negra. En 1957 también, Menéndez y coautores,<sup>3</sup> usando la técnica de la electroforesis de hemoglobina en papel, encuentran que un 2.6% de los casos presentan la hemoglobina S, sola o combinada con la hemoglobina A, y en raras ocasiones, con la hemoglobina C. En 1959 Suárez y colaboradores<sup>4</sup> utilizan la electroforesis en papel y el cromio radioactivo (Cr 51) para estudiar el promedio de vida de los hematíes, reportando una proporción de hemoglobinas anormales de 2.1% si se consideraba la población total y de 6.81% cuando el estudio incluía solo a la raza negra. La hemoglobina anormal más frecuente fue desde luego la S, aunque la C, sola o combinada, fue identificada en el 1.33% de la población. La hemoglobina fetal (F) no fue señalada como presente. En 1962, Torregrosa<sup>5</sup> reportó un caso de talasemia mayor (anemia de Cooley) o hemoglobina F homozigótica, aunque la genética del caso no estaba entonces completamente terminada.

La incidencia de las hemoglobinas anormales en los demás países del Caribe es muy semejante a la informada en Puerto Rico, cosa fácil de explicar dada la analogía de los primeros pobladores y de la subsiguiente immigración. Uno de nosotros, (G.P.) trabajando exclusivamente con el fenómeno de la drepanocitosis

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provocada, encontró en 1939<sup>6</sup> que un 5.3% de la población negra de Cuba presentaba drepanocitosis en forma activa o heterozigótica.

Los trabajos más acuciosos han sido realizados en Jamaica donde Went, Mac Iver e Irvine<sup>7-11</sup> han informado, no solamente la incidencia de drepanocitosis, sino de sus combinaciones anormales. Estos autores encontraron además una predominancia de la hemoglobina F (fetal) tan alta como en el 3.2% de la población, en la forma de talasemia menor. La combinación de la drepanocitemia con la talasemia menor (drepanocitemia-talasemia), entidad que ha inspirado esta comunicación, fue informada en 11 casos de estos autores.

La drepanocitemia-talasemia o microdrepanocitosis ("sickle-cell--thalassemia") es conocida desde 1946<sup>12</sup> y desde entonces han aparecido un número apreciable de trabajos sobre esta condición.<sup>13-16</sup> Sin embargo, una revisión de la literatura hematológica de Puerto Rico no reveló ningún informe previo de esta entidad aquí. Es por esto que nos ha parecido de interés informar una familia con cinco de sus miembros afectados por microdrepanocitosis, uno de los cuales será informado en detalle para ilustrar el cuadro clínico de esta enfermedad.

#### HISTORIA CLINICA

E.P.C., caso 40739, un paciente varón, fue admitido por primera vez al antiguo Hospital de Distrito de Ponce en abril de 1954 a la edad de seis años, aquejando mareos, cansancio y dolores abdominales. El historial previo reveló ataques repetidos de infecciones respiratorias. El examen físico demostró un niño pálido, enfermizo, con marcada protuberancia del abdomen. Pesó 37½ libras y tenía 42 pulgadas de estatura; la temperatura era de 37.8°C, el pulso 108 y la respiración 16 por minuto. Se observó un tinte subictérico de la esclerótica y palpación del abdomen demostró un gran aumento en el tamaño del bazo, que se extendía hasta la fossa iliaca izquierda. Los exámenes de laboratorio revelaron una hemoglobina de 3.19 gramos% (22%), con 1.03 millones de hematies y 8,8×10 glóbulos blancos. La serología fue negativa y las heces fecales revelaron ascariasis y trichiuris.

En esa primera admisión se le administraron dos transfusiones de sangre, extracto de hígado y tiamina, dándosele de alta con una hemoglobina de 6.0 gramos% y un diagnóstico final de "síndrome de Banti" y parasitosis intestinal.

Sus dos admisiones subsiguientes fueron también en el viejo Hospital de Distrito en Diciembre de 1954 y en 1955. En ambas ocasiones fué admitido por anemia severa y crisis abdominales

dolorosas. El tratamiento consistió en la administración de sangre, hematínicos y elixir paregórico.

La cuarta hospitalización fue en abril de 1956 en el Departamento de Pediatría del Hospital de Distrito de Ponce "José N. Gándara", por una masa en el cuadrante superior izquierdo, marcada palidez y tinte ictérico de la esclerótica. Fue en esta ocasión que se estableció el diagnóstico de anemia drepanocítica cuando una preparación especial demostró 100% de células falciformes ("sickles cells"). El contaje de reticulocitos fue de 4.4%, la hemoglobina 5.5 gm.% y la bilirrubina sérica 1.7 mg.% con una fracción indirecta de 1.0 mg.%. Las plaquetas estaban moderadamente disminuidas (100,000) y la aspiración de médula ósea reveló solamente una hiperplasia eritroide marcada, de tipo normoblástico.

En noviembre de 1957 el paciente fue admitido por quinta vez, administrándosele 500 cc. de sangre; se le dió de alta con una hemoglobina de 50% y fue referido a clínicas externas.

El paciente fué readmitido en octubre 18, 1960, esta vez al Departamento de Medicina, a la edad de 12 años. En ocasiones anteriores había llamado la atención la persistencia de la marcada esplenomegalia a pesar de las crisis abdominales que sugerían episodios trombóticos que se esperaba produjeran una gradual atrofia del bazo. Se consideró la posibilidad de una trombosis de la porta o esplénica, o una combinación de hemoglobinopatía C con anemia drepanocítica. Para eliminar una trombosis de la vena porta se practicó un esplenoportograma con excelente visualización de la vena esplénica y la porta, sin evidencia de obstrucción extrahepática.

Su séptima hospitalización en marzo de 1961 fue motivada por anemia severa que requirió cuatro transfusiones más. Al observarse muchas células en diana ("target cells") se hizo una electroforesis de su hemoglobina, la cual mostró solamente hemoglobina S.

En vista de la marcada esplenomegalia y la posibilidad de que mejorara la tendencia hemolítica, se recomendó una esplenectomía, procedimiento que ha sido beneficioso en pacientes de anemia drepanocítica con hiperesplenismo.<sup>17-20</sup> Esta fue practicada en mayo 5, 1961. La operación se vió complicada en los días siguientes por una trombocitemia (954,000 plaquetas) que provocó un infarto pulmonar. Estas complicaciones fueron tratadas con terapia de anticoagulantes y el paciente mejoró, siendo dado de alta en condiciones satisfactorias, aunque con hemoglobina de solo 8.5 gm.% (58%).

Desde entonces, el paciente ha tenido siete admisiones adicionales, desde 1961 hasta diciembre de 1963. Estas han sido por crisis hemolíticas que han requerido transfusiones repetidas, y gran

tendencia a infecciones secundarias, atribuídas en parte a la esplenectomía.<sup>21</sup>

En su última admisión en diciembre de 1963, se consideró la posibilidad de que fuera éste un caso de drepanocitemia-talasemia y esta impresión clínica fue definitivamente establecida por estudios específicos incluídos en la tabla 1.

El análisis de la familia de este primer caso nos permitió diagnosticar cuatro adicionales. Los padres (A.P. y J.C.R.) son ambos puertorriqueños; él es aparentemente blanco y ella muestra rasgos discretos de mestiza. Los dos alegaron descender de españoles (ella cree que entre sus antepasados había corsos y él que entre los suyos hay descendencia india.) Han tenido 19 hijos de los cuales han muerto seis; uno de ellos con historial sugestivo de padecer de la enfermedad bajo discusión y los demás por causas no relacionadas. De los 13 hijos restantes hemos podido examinar siete. De estos, dos (E.C.P., caso 1, antes descrito y H. P., caso 2) sufren del tipo severo de drepanocitemia-talasemia y tres (casos 3, 4, y 5) poseen las características hematológicas de la afección. Los casos 3 y 4 tienen anemia moderada y el 5 no ha desarrollado complicaciones hasta ahora apesar de tener la condición. Los otros dos hermanos estudiados dieron resultados negativos.

**Comentarios:** Este paciente presentó datos clínicos y hematológicos diferentes a los usualmente encontrados en anemia drepanocítica. Esto sugirió la posibilidad de una hemoglobinopatía C combinada con drepanocitemia (enfermedad S-C), pero esta sospecha fue desechada después de que el estudio electroforético de la hemoglobina demostró que su movilidad era de hemoglobina S solamente. La presencia de gran cantidad de hematíes en diana en la lámina periférica y la ausencia de drepanocitosis en el padre debió sugerirnos la posibilidad de la drepanocitemia-talasemia. Sin embargo, no se pensó en esta condición hasta revisar la excelente descripción que de la misma hicieron recientemente Kone-man, Miale y Hanson.<sup>16</sup> A la gentileza del Dr. Miale debemos algunos de los estudios más importantes realizados a esta familia y los cuales se hicieron en el Jackson Memorial Hospital de Miami. La conclusión del Dr. Miale fue: "que el padre es un caso de talasemia menor, que la madre tiene drepanocitemia heterozigótica y que genéticamente los hijos pueden ser todos casos de drepanocitemia-talasemia por posible interacción de las cadenas beta."

#### DISCUSION

Los trabajos basados en la movilidad electroforética de las diferentes hemoglobinas han hecho factible la identificación de una serie de entidades que desde entonces se han denominado hemo-

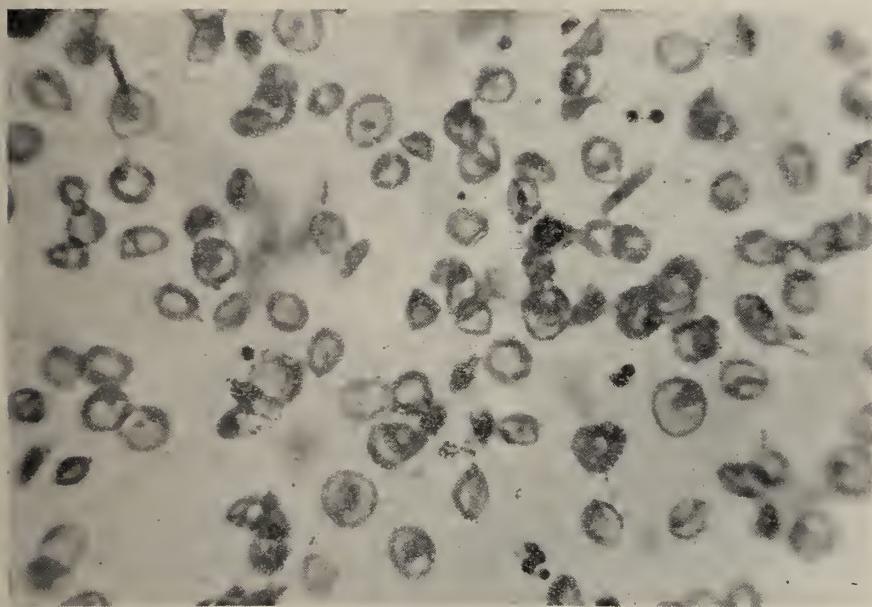


FIGURA 1

Fotografía de lámina de la sangre periférica del caso de drepanocitemia talasemia, demostrando microcitosis, hipocromia, gran cantidad de células en diana, drepanocitos y un normoblasto en el centro.

globinopatías. Empezando por la hemoglobina S (derivada de "sickle") se han descrito más de 20 variedades que pueden ser diferenciadas de la hemoglobina normal del adulto (hemoglobina A.) Los trabajos posteriores de Ingram<sup>22-24</sup> mediante la fragmentación de los nucleoproteídos de la molécula de globina en cadenas de aminoácidos y proteídos de la molécula de globina en cadenas de aminoácidos y su electroforesis y cromatografía posterior por la técnica conocida como de impresiones digitales, definitivamente demostraron que los distintos tipos de hemoglobina encontrados en la electroforesis en papel o por otras técnicas, eran realmente producidos por la substitución de alguno de los aminoácidos de las cadenas por otros. Se pudo comprobar que la diferencia entre la hemoglobina A del adulto normal y la S de la drepanocitemia se debe a la substitución de una molécula de ácido glutámico en las cadenas beta por una molécula de valina, en tanto que si la substitución se realiza por una molécula de lisina, la hemoglobina resultante es la C. Así sucesivamente resulta con las demás hemoglobinas.<sup>25,26</sup>

Se puede clarificar más este concepto si recordamos que la estructura química de la molécula de hemoglobina se compone del heme (cuatro núcleos pirrólicos y un átomo de hierro) y de la globina. Esta última está compuesta a su vez de cuatro cadenas de

TABLA I  
RESUMEN DE ESTUDIOS HEMATOLOGICOS

Caso	Edad	Sexo	Hematíes Millones (gm.%)	Hb.	Drepanocitos en lámina	Dianas en lámina	Drepanocitos Provocada	Electroforesis en papel	Hb. Fetal <sup>1</sup>	Hb. A <sub>2</sub> <sup>2</sup>	Fragilidad Globular <sup>3</sup>
Padre: AP	52	M	5.5	11	No	10%	No	Hb. A	2.3%	4.6%	0.40—0.15
Madre: JRC	49	F	4.5	12.8	No	No	70%	Hb. A y S	1.6%	---	0.45—0.30
#1* E.P.	16	M	2.6	7.2	5%	25%	100%	Hb. S	3.9%	1.0%	0.30—0.15
#2* H.P.	25	M	3.0	8.3	6%	30%	100%	Hb. S	4.3%	0.5%	0.30—0.15
#3* M.J.P.	8	F	3.1	7.8	4%	50%	100%	Hb. S	5.4%	1.6%	0.30—0.15
#4* L.S.P.	11	M	3.3	8.4	3%	10%	100%	Hb. S	4.7%	2.1%	0.30—0.15
#5* C.J.P.	9	F	4.1	10	No	8%	100%	Hb. S	3.7%	---	0.40—0.20
J.R.P.	9	M	4.8	12	No	No	No	Hb. A	1.4%	---	0.45—0.30
R.P.	8	M	5.1	13	No	No	No	Hb. A	1.1%	---	0.45—0.30

\* Casos de drepanocitemia-talasemia

1. Hb. fetal normal = menos de 2%
2. Hb. A<sub>2</sub> normal = menos de 3%
3. Fragilidad globular normal: empieza — 0.45—0.39%  
Completa — 0.33—0.30%

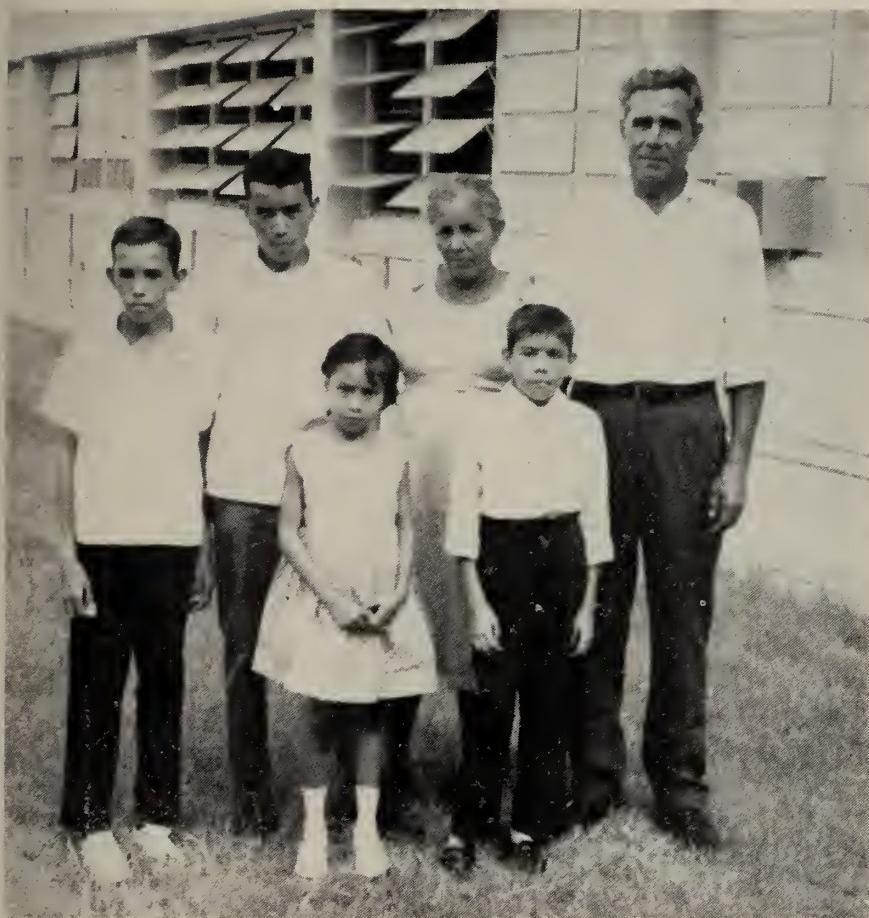


FIGURA 2

Fotografía de familia informada. En la primera fila vemos de izquierda a derecha el caso 3 (M.L.P.) y el 4 (L.S.P.) y en la segunda fila el caso 1 (E.P.) y el 2 (H. P.) y los padres. No fue retratado el caso 5 (C.J.P.)

polipéptidos, de los cuales dos se denominan cadenas alfa y las otras dos, cadenas beta. Las cadenas alfa son formadas por 141 aminoácidos que terminan en la secuencia: valina-leucina-serina; por otro lado, las cadenas beta están constituidas por la secuencia de 146 aminoácidos que terminan en valina-histidina-leucina. El peso molecular de cada cadena alfa es de 15,126 mientras que el de las cadenas beta es de 15,936. La suma total de las cuatro cadenas de polipéptidos y el heme hace un peso molecular para la molécula de hemoglobina de 64,450, muy cercano al de 64,500 obtenido por ultracentrifugación. Como se mencionó antes, las variaciones de la movilidad electroforética se deben a substitución de un aminoácido por otro; cuando estas hemoglobinas son sometidas a cambios en su combinación con el oxígeno, o en el pH del

medio, adquieren propiedades especiales (tactoides) y alteraciones en la solubilidad que originan las manifestaciones clínicas de las hemoglobinopatías.

El concepto de que la hemoglobina normal (hemoglobina A) era un componente homogéneo fue modificado por los trabajos de Kunkel y Wallenius.<sup>27</sup> Estos investigadores demostraron la existencia de una segunda y pequeña fracción de escasa movilidad electroforética demostrable por técnicas especiales como la del gel de almidón, papel de acetato y el milipore, pero no por la electroforesis en papel. Al estudiarse esta fracción, que fue denominada hemoglobina A2, por medio de la técnica de las impresiones digitales, se encontró que sus cadenas beta estaban substituidas por una secuencia especial de aminoácidos designada cadena delta. La proporción de hemoglobina A2 en personas normales es inferior al 2% de la hemoglobina total pero en la talasemia menor esta fracción está usualmente elevada. Kunkel y sus asociados<sup>28</sup> analizaron 34 pacientes con talasemia menor, encontrando 32 con un aumento en hemoglobina A2 sobre 3.5%. Por otro lado, en la familia que acabamos de informar, sólo el padre tuvo una hemoglobina A2 anormal, aunque la fetal (F) estuvo aumentada, tanto en el padre como en los cinco hijos con microdrepanocitosis (véase tabla 1). Un nivel normal o bajo de Hb. A2 no elimina el diagnóstico de talasemia.<sup>16</sup>

La hemoglobina fetal (F) heterozigótica constituye al nacer más del 70% de la hemoglobina total, pero disminuye rápidamente siendo substituida por la A; al final del primer año la cantidad de hemoglobina F es menos del 2%. Sus características generales incluyen una más eficiente transportación de oxígeno que la hemoglobina adulta, una mayor susceptibilidad a convertirse en metahemoglobina y una mayor resistencia a la denaturalización por los alcalis. También se ha demostrado por el método de las impresiones digitales diferencias en la estructura de su molécula de globina, ya que presenta una secuencia de aminoácidos en las cadenas beta distintas a las de la adulta, siendo denominadas cadenas gama.

La persistencia de la hemoglobina F en niveles por encima del 70% de la hemoglobina total constituye la forma homozigótica (FF) de la talasemia o talasemia mayor, conocida también como anemia del Mediterráneo por su alta incidencia en los países circundantes al mismo.

La forma heterozigótica (AF) o talasemia menor, ilustrada por el padre de la familia informada antes, es la que posee, además de un aumento moderado de hemoglobina fetal, un aumento en la fracción A2. Cuando esta forma heterozigótica de talasemia (con cadenas delta de la A2 y gama de la hemoglobina F) se une a la forma heterozigótica de la hemoglobina S o la C, se produce una

anulación de las propiedades electroforéticas de la hemoglobina A y de la F, manifestándose como casos puros de hemoglobina S. Se cree que esto se debe a la interacción de las cadenas delta y gama sobre las cadenas beta de la hemoglobina A. Como ocurrió en el caso de microdrepánocitosis nuestro, (caso 1) al realizarse un estudio electroforético en papel la movilidad será de hemoglobina S y el paciente parecerá ser simplemente un caso de drepánocitemia. Went, Mac Ivert e Irvine<sup>7</sup> han sugerido que la hemoglobina F ocupa un lugar (*locus*) idéntico al de la S y C, y distante al de la A, lo cual explicaría la facilidad para adquirir una forma aparentemente homozigótica a los alelos S y C y no al alelo A que ocupa un lugar más distante.

Las características de la drepánocitemia-talasemia incluyen manifestaciones de ambas entidades, es decir, de talasemia menor y drepánocitosis. La talasemia menor producirá:

1. Presencia de hematíes en diana en número variable, pero siempre abundante.
2. Una hipocromia manifiesta, con o sin microcitosis predominante.
3. Una cifra normal o exagerada del número de hematíes.
4. Un aumento de la resistencia de los hematíes a las soluciones hipotónicas que puede llegar a 0.
5. Un aumento en la hemoglobina fetal (demostrable por la resistencia a la denaturalización a los alcalis) y de la hemoglobina A2 (demostrable por la electroforesis en gel de almidón).
6. Hierro sérico elevado o normal.

A estos se unen los signos hematológicos y clínicos de la drepánocitemia:

7. Presencia de drepánocitos en número variable.
8. Drepánocitemia provocada de 100%.
9. Electroforesis de hemoglobina en papel de tipo S homozigótico.
10. Desde el punto de vista genético: Ausencia de hemoglobina S en uno de los progenitores, lo cual haría prácticamente imposible la drepánocitemia homozigótica.

Aunque la microdrepánocitosis ha sido descrita como más benigna que la drepánocitemia homozigótica, por lo menos dos de los casos informados en esta comunicación han seguido un curso clínico que compara con los más severos que se observan en anemia drepánocítica. Es posible que la severidad relativa dependa de la mayor o menor penetración del gene S.

## RESUMEN

1. Se ha revisado la literatura local y la del área del Caribe sobre las hemoglobinopatías.
2. Se han informado cinco casos de drepanocitemia-talasemia; estos casos constituyen los primeros descritos en Puerto Rico.
3. Se ha hecho una revisión de la patogenia de la condición, así como de los hallazgos clínicos y hematológicos.
4. Es nuestra impresión que esta familia no constituye un hecho aislado en nuestra isla y que posiblemente otros casos clasificados hasta ahora como de drepanocitemia y otros aún no estudiados resulten ser casos de microdrepanocitos.

## SUMMARY

1. Sickle cell-thalassemia (Microdrepanocytic disease) is a disease caused by a double heterozygotic state through an interaction of the inherited sickle cell gene from one parent and that of thalassemia from the other.
2. This paper deals with a report of the first five cases of this condition in Puerto Rico. The pathogenesis of sickle cell-thalassemia and the clinical and hematologic aspects of the disease have been discussed.
3. It is the impression of the authors that this family does not constitute an isolated finding in the island but that possibly other cases diagnosed as sickle cell anemia and others not yet studied may well be further examples of the condition.
4. The value of such studies as peripheral blood smear, filter paper and starch block electrophoresis, and of the determination of alkali-resistant hemoglobin in the diagnosis of sickle cell-thalassemia has been stressed. The study of the parents of suspected cases is of vital importance.

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## LA EMBOLIA PULMONAR AGUDA.

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**ETIOLOGIA:** La mayoría de las embolias pulmonares tienen su origen en el desprendimiento de trombos que se forman en las venas periféricas. Siendo éste el factor etiológico de mayor importancia una descripción breve de la tromboflebitis y de la flebotrombosis está en orden.

La causa precisa de la tromboflebitis es desconocida. La lentitud de la corriente sanguínea parece ser un factor importante en la formación del trombo. El aceleramiento del tiempo de coagulación probablemente entra en juego. El papel de las alteraciones en las paredes de los vasos no ha sido determinado. Apesar de las manifestaciones sistémicas severas y de la evidencia de reacción inflamatoria en las extremidades en los casos más fulminantes, ningún agente infeccioso ha sido hallado.

La formación de trombo en las venas es frecuente. Las venas varicosas superficiales, dilatadas y tortuosas comúnmente se convierten en duras y dolorosas, con enrojecimiento de la piel superyacente. La reacción inflamatoria usualmente termina sin consecuencias, y las complicaciones embólicas son más bien raras. La trombosis recurrente de las venas profundas o superficiales ocurren con frecuencia durante la evolución de la enfermedad oclusiva arterial. El trauma local producido por la administración de varias soluciones y medicamentos es una causa frecuente de tromboflebitis superficial. Nuevamente, los fenómenos embólicos son raros. La formación de trombo en las venas ocurre a veces durante las infecciones agudas y crónicas, después de operaciones y partos. Es común en pacientes con debilitamiento crónico, fallo cardíaco o carcinomatosis, y ocasionalmente ocurre en personas aparentemente normales.

La trombosis venosa es propensa a ocurrir en áreas contiguas a infección local o trauma. Se ve en la pelvis durante la infección puerperal y en las venas prostáticas después de la prostatectomía. En la mayoría de los casos, el trombo comienza en las venas profundas de la pantorrilla y se extiende proximalmente. El envolvimiento de las venas del muslo y de la pelvis conlleva el riesgo más grande de embolización. El hecho de que el trombo en las venas del muslo no sea necesariamente oclusivo podría explicar la ausencia frecuente de manifestaciones clínicas. La mayoría de las embolias pulmonares aparecen dentro de las primeras semanas después del desarrollo de la trombosis venosa. Las embolias que aparecen algu-

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nos meses después del episodio trombótico inicial son atribuibles a un trombo nuevo o a extensión del trombo original. La importancia clínica de la embolia pulmonar depende de su tamaño y multiplicidad. El proceso puede causar una pequeña reacción en la pared venosa (flebotrombosis) y si éste es el caso, el trombo es particularmente propenso a desprenderse y alojarse en el árbol pulmonar. Por otra parte, la reacción puede envolver las venas de toda una extremidad, con una reacción inflamatoria que se extiende dentro de los canales linfáticos circunvecinos (tromboflebitis). Cuando así sucede, existe una reacción extensa, el cóagulo se adhiere íntimamente a la pared venosa, y los fenómenos embólicos son bien raros.

Los síntomas locales pueden estar ausentes. Un aumento en la frecuencia del pulso o una fiebre ligera sin explicación en un paciente en cama pueden ser los únicos signos de flebotrombosis y la condición puede no ser reconocida hasta que un émbolo se aloja en la arteria pulmonar. Algunos días más tarde, sensibilidad en una o ambas pantorrillas puede aparecer. La sensibilidad en la pantorrilla y el dolor en la misma a la dorsiflexión del pie pueden ser los únicos signos.

Si la pierna está dependiente, cianosis y edema ligero pueden ser observados. Otros hallazgos pueden incluir un measurable aumento, aunque no siempre visible, en la circunferencia de la pantorrilla cuando se compara con la pierna opuesta, prominencia ligera de las venas, aumento de calor local o pulsaciones disminuidas en el lado afectado, y dolor local a la compresión con un esfigmomanómetro a una presión de 80 a 120 mm. Hg.

En el otro extremo hallamos la pierna dolorosa, hinchada y cianótica de la tromboflebitis aguda. En esta condición, las arterias no están envueltas directamente; sin embargo, puede ocurrir un reflejo vasoconstrictor intenso, que hace en ocasiones difícil la palpación del pulso arterial. Usualmente hay fiebre y leucocitosis.

Además de la flebotrombosis y de la tromboflebitis como causas principales de la Embolia Pulmonar Aguda existen algunas otras condiciones, aunque menos comunes que ocasionan embolia pulmonar. Dichas condiciones las mencionaremos someramente. El aire puede entrar en el sistema vascular como consecuencia de una toracentesis o en operaciones con "corazón abierto". Bajo tales circunstancias la embolia compromete los vasos sistémicos más que los pulmonares, y las manifestaciones principales generalmente son oclusión arterial coronaria o cerebral.

La embolia pulmonar puede ocurrir como resultado de errores técnicos durante la terapia intravenosa o por rotura de una vena

cervical durante una intervención quirúrgica. El líquido amniótico con sus restos puede causar embolia durante el parto.

La embolia grasa es usualmente el resultado de fractura del fémur o de otros huesos largos. Sin embargo, la misma puede ocurrir como resultado de lesión de los pequeños huesos o aún del tejido blando adiposo. Cuando es el resultado de la esternotomía en pacientes durante la cirugía cardíaca o derivación cardiopulmonar, la ausencia transitoria de la función filtrante de los pulmones aumenta la probabilidad de la embolia grasa cerebral. Las manifestaciones pueden ser principalmente sistémicas o pulmonares como resultado del paso de masas grasosas a través de los capilares del pulmón, con embolia en varios órganos. La presencia de glóbulos grasos en las arterias retinianas, en el esputo, y especialmente en la orina pueden ofrecer la clave hacia el diagnóstico. Este último es frecuentemente difícil ya que el cuadro clínico puede ser raro y parecerse a enfermedad del colágeno o a otro desorden sistémico. En algunos casos, las manifestaciones principales son aquellas de una enfermedad aguda multifocal del sistema nervioso central. El diagnóstico de la embolia grasa usualmente no se dificulta si uno piensa en su posibilidad en un enfermo que presenta evidencia de enfermedad sistémica o pulmonar rara después de un trauma.

La embolia pulmonar, al igual que la de otros órganos, puede ocurrir durante la crisis aguda de la enfermedad Sclémica.

Las enfermedades primarias del miocardio frecuentemente causan tromboembolismo de las circulaciones pulmonar y sistémica al igual que fallo cardíaco rebelde a tratamiento el cual usualmente termina el curso en los casos crónicos.

Una de las complicaciones más serias de las enfermedades del corazón es la embolia pulmonar. Aunque el origen del émbolo es usualmente en las extremidades inferiores, se sabe ahora que el corazón mismo es más frecuentemente el lugar de origen que lo que anteriormente se creía. El trombo intracardíaco muy a menudo se forma en el lado izquierdo del corazón y el émbolo cuando se libera va a través de la circulación sistémica obstruyendo las pequeñas arterias de las extremidades, vísceras y cerebro. Sin embargo, la formación de trombos murales en el lado derecho del corazón no es rara. Los mismos ocurren cuando la trombosis coronaria produce infarto septal o ventricular derecho. La endocarditis bacteriana o la verrucosa como en la Enfermedad de Libman-Sacks pueden dar origen a émbolos múltiples los cuales se alojan en los pulmones. En la fibrilación atrial especialmente cuando está asociada con la estenosis mitral, las corrientes sanguíneas en remolino pueden formar coágulos en el dilatado apéndice auricular derecho los cuales encuentran su camino hacia los pulmones.

El estado de "shock" con dilatación cardíaca y presión arterial baja por tiempo prolongado como se ve después de la oclusión de un vaso coronariano grande tiende a la formación de trombos. Estos pueden desprenderse y convertirse en émbolos en la circulación pulmonar.

**INCIDENCIA.** La embolia pulmonar se encuentra en alrededor del 10 por ciento de todas las autopsias, y ocasiona de 2 a 3 por ciento de las muertes. 40 por ciento de las embolias pulmonares ocurren durante el estado postoperatorio, 30 por ciento en pacientes cardíacos y 30 por ciento en pacientes médicos no-cardíacos. La embolia pulmonar resulta en el infarto en 60 por ciento en los casos no cardíacos, y en 90 por ciento en los cardíacos. 80 por ciento de las embolias en los casos no cardíacos provienen de la tromboflebitis. En los cardíacos, alrededor del 25 por ciento resultan de trombos cardíacos intramurales, principalmente del atrio derecho.

En la serie de Hampton y Castleman, el 74 por ciento de las embolias estaban localizadas en los lóbulos inferiores, 43 por ciento de las mismas en el derecho y el 31 por ciento en el izquierdo; el resto, 26 por ciento estaban distribuidas más o menos igual en los otros lóbulos.

**Sexo y edad.** La embolia pulmonar puede ocurrir desde el joven hasta el viejo, pero la mayoría de los casos se ven en los pacientes que sobrepasan los 40 años. De acuerdo con Barker y sus asociados la mayoría de los casos ocurren entre los cuarenta y sesenta años en las mujeres, y entre los cincuenta y setenta años en los hombres.

**Factores precipitantes.** No es infrecuente que los síntomas de la embolia pulmonar aparezcan durante o inmediatamente después del esfuerzo al evacuar, al levantarse de la cama, o bien al abordar o salir de una silla de ruedas. Es muy probable que estos factores ayuden en el desprendimiento del trombo dentro de la circulación.

**FISIOLOGIA PATOLOGICA.** La anoxia arterial y la cianosis son síntomas frecuentes de la embolia pulmonar. Ambas no están completamente bien entendidas. Se sabe que una circulación anastomótica con las arterias bronquiales se produce prontamente; pueden ocurrir también comunicaciones arterio-venosa pulmonar. La disnea taquipneica del tipo hiperneico, está probablemente asociada a la embolia masiva pulmonar han sido atribuídos a: 1. La intercambio está presente es debido en parte al fallo del retorno venoso al corazón izquierdo, y en parte al desorden general en el tono vaso-motor. Cuando hay embolias pulmonares múltiples, el síndrome de fallo cardíaco agudo o crónico puede desarrollarse.

**PATOGENESIS DE LAS SECUELAS CIRCULATORIAS Y CARDIACAS.** Los desórdenes circulatorios y cardíacos que siguen a la anoxia; pueden ocurrir "reflejos" y otros factores. El "shock"

ferencia mecánica con el vaciado cardíaco, y 2. La isquemia del miocardio.

1. La embolia masiva interfiere brúscamente con el vaciado del corazón derecho, en consecuencia hay una disminución en la afluencia de sangre y en el vaciado del ventrículo izquierdo, de suerte que la presión aórtica se reduce marcadamente y la evidencia de "shock" aparece. Al mismo tiempo, la resistencia pulmonar aumenta, lo que ocasiona un mayor esfuerzo del ventrículo derecho, conduciendo esto último a la dilatación y quizás al fallo retrógrado del corazón derecho. Esto demuestra que los diversos trastornos circulatorios resultan únicamente después de que una mayor parte del área transversal de la circulación pulmonar es ocluida, y que la seriedad de los efectos circulatorios es aproximadamente proporcional al grado de oclusión, de suerte que existe una fuerte evidencia para creer que la obstrucción mecánica de la circulación es la causa primaria y directa de las secuelas circulatorias que siguen a la embolia pulmonar masiva.

2. La isquemia del miocardio ha sido invocada en la explicación de la muerte violenta en algunos casos, y al mismo tiempo para explicar algunas similitudes en los cuadros clínicos y electrocardiográficos de la embolia pulmonar y el infarto agudo del miocardio. Tres mecanismos podrían dar cuenta de la ocurrencia de la isquemia del miocardio que siguen a la embolia pulmonar: A. La embolia pulmonar misma causa una reducción en la presión aórtica y vaciado del ventrículo izquierdo, con una disminución correspondiente en el suministro sanguíneo a las arterias coronarias. B. La anoxia arterial debido a la asfixia pulmonar puede producir anoxemia del miocardio. C. El reflejo vasoconstrictor de las arterias coronarias, mediado por el nervio vago (reflejo pulmón-coronario) ha sido señalado para explicar la ocurrencia de la muerte violenta, en los casos que había solamente una embolia pulmonar pequeña. Receptores para reflejos vagales han sido demostrados en la arteria pulmonar. Experimentalmente, la vagotomía preliminar o la administración de atropina dió paso a una alta incidencia de supervivencia en animales que habían sido inyectados con dosis letales de émbolos pulmonares. Sin embargo, otros experimentos no han sustanciando estos hallazgos y han fallado en sustentar la teoría de que la muerte por embolia pulmonar es debida a reflejos pulmonares al corazón o al centro respiratorio.

Los serios desórdenes circulatorios o la muerte que siguen a una embolia pulmonar relativamente pequeña han sido explicados bajo la suposición de que un reflejo vasoconstrictor local aumenta el efecto oclusivo de la embolia. Esto es análogo a la bien conocida vasoconstricción que sigue a la embolización de una arteria peri-

férica en una extremidad. Sin embargo, mientras exista un fuerte control vasomotor de los vasos periféricos habrá un desacuerdo considerable en cuanto a la importancia de los efectos vasomotores en los vasos pulmonares.

El flujo sanguíneo coronariano puede estar limitado como consecuencias del aumento en la presión en el corazón derecho después de la embolia pulmonar. Este aumento en la presión intraventricular disminuye la presión coronaria efectiva y empeora el drenaje por medio de los vasos Thebesianos. Cualquiera que sea la causa de la isquemia del miocardio en los casos de embolia pulmonar masiva, su ocurrencia aparece substanciada por los estudios clinicopatológicos de Friedberg, et al. En 8 de 42 casos autopsiados de embolia pulmonar estos últimos observadores hallaron necrosis aguda y subaguda del miocardio, semejante a aquellas del infarto agudo del miocardio debido a oclusión coronaria reciente. Los cambios estructurales más severos fueron encontrados en la región subendocárdica del ventrículo izquierdo, los mismos fueron interpretados como debidos a la isquemia del miocardio cuando ésta fue suficientemente prolongada y severa.

El desarrollo de la necrosis fue favorecida por una prolongación de la vida por varias horas o semanas después de la embolia inicial, por estrechamiento o esclerosis coronaria existente, y por hipertrofia cardíaca previa lo cual acentúa la insuficiencia coronaria. Sin embargo, en 3 casos la necrosis del miocardio ocurrió en ausencia de estrechamiento significativo de las arterias coronarias.

**MANIFESTACIONES CLINICAS.** Un émbolo único induce un estado que imita bien de cerca el cuadro clínico del infarto del miocardio. No es extraño que el dolor tenga la misma localización subesternal al igual que el mismo sea de tipo constrictivo. Es probablemente debido al resultado de la hipoxia del ventrículo derecho porque tanto el aumento de la presión sistólica en dicho compartimiento como la caída de la presión sistémica arterial disminuyen el flujo coronario al ventrículo derecho. Otros síntomas que son similares son disnea, distención venosa, y muerte violenta. Ambas condiciones son seguidas frecuentemente por una elevación transitoria del contejo leucocitario, temperatura y sedimentación de los eritrocitos. Las alteraciones electrocardiográficas (patrón de "sobrecarga ventricular derecha" consistiendo en depresión del segmento ST en derivaciones I, II, III, AVF, V<sub>2</sub> y V<sub>3</sub>) pueden ser similares en las dos condiciones. Finalmente, aunque el infarto pulmonar por sí mismo no causa mucha elevación de la transaminasa, la lesión muscular asociada con la coexistente (y a menudo silenciosa) tromboflebitis puede causar elevación marcada. Cuando la evidencia del pro-

ceso trombótico local en las venas está ausente, y cuando la comparación del aire expirado terminal y la tensión del bióxido de carbono en la sangre arterial no dan información decisiva, la distinción entre la embolia pulmonar y el infarto del miocardio puede ser casi imposible. Sin embargo, la combinación de una dehidrogenasa láctica elevada, de una transaminasa normal, y una bilirrubina sérica elevada sugieren fuertemente un infarto pulmonar.

Esta combinación de elevación de la dehidrogenasa láctica sérica, aumento en la concentración de la bilirrubina sérica y actividad normal de la transaminasa glutámica oxalacética sérica en el diagnóstico de la embolia pulmonar con infarto fué objeto de un estudio reciente por Wacker, Rosenthal, Snodgrass y Amador. Ellos estudiaron tres grupos de pacientes. El grupo 1 incluyó cinco pacientes con embolia o infarto pulmonar demostrado con autopsia; el grupo 2 comprendió doce pacientes con evidencia clara de infarto pulmonar, y el grupo 3 incluyó siete pacientes que mostraron en la autopsia haber muerto de infarto agudo del miocardio o de pulmonía bacteriana.

En todos los pacientes del grupo 1 la actividad sérica de la dehidrogenasa láctica se halló elevada; en cuatro de cinco, la actividad de la transaminasa oxalacética glutámica fue consistentemente normal; y en tres de cuatro en los cuales fue determinada la concentración de la bilirrubina se encontró elevada. Todos los pacientes en el grupo 2 tenían elevación de la dehidrogenasa láctica sérica los primeros ocho días después del comienzo de los síntomas y una transaminasa glutámica oxalacética sérica normal los primeros cuatro días después del comienzo del infarto. La concentración de la bilirrubina sérica determinada en once pacientes, se encontró elevada en ocho. En el grupo 3, los valores de la dehidrogenasa láctica sérica, la transaminasa glutámica oxalacética y los valores de la bilirrubina fueron normales en dos pacientes que murieron de pulmonía bacteriana masiva. Cinco pacientes que murieron de infarto agudo del miocardio mostraron el aumento usual en la dehidrogenasa láctica sérica al igual que la transaminasa glutámica oxalacética. La bilirrubina sérica fue determinada en tres de estos pacientes hallándose normal en dos y elevada a 1.9 mg./100 cc. en uno, cuyo curso clínico se complicó con un infarto esplénico.

En el infarto pulmonar cualquiera de las dos fracciones de la bilirrubina, es decir, la directa o la indirecta pueden hallarse elevada. Si hay congestión aguda del hígado como resultado de la embolia pulmonar y un aumento brusco en la presión venosa, una elevación de la fracción reactiva-directa podría ocurrir; por otra parte, la absorción de sangre de un infarto pulmonar puede ocasionar una elevación de la fracción indirecta. La dehidrogenasa láctica sérica

se encontró uniformemente elevada en los pacientes con embolia e infarto, subiendo frecuentemente durante el primer día, alcanzando un máximo durante el segundo día y descendiendo a lo normal dentro de 10 días. Hubo una elevación consistente de la dehidrogenasa láctica en los diez pacientes probados con autopsia y en 21 pacientes con evidencia clínica y de laboratorio de infarto pulmonar. Un aumento de la bilirrubina sérica después del infarto pulmonar ocurrió en once de quince pacientes en los cuales la misma fue determinada. La transaminasa glutámica oxalacética sérica se mantuvo permanentemente normal en la mayoría de los pacientes.

La diferenciación inequívoca entre el infarto del miocardio y la embolia pulmonar requiere determinaciones seriadas de los tres parámetros descritos comenzando dentro de los primeros dos días después del inicio de los síntomas.

En un estudio clinicopatológico de 100 casos de Embolia masiva de la Arteria Pulmonar Gorham menciona doce signos físicos que el cree son de gran ayuda en el diagnóstico diferencial con el Infarto Agudo del Miocardio. Estos signos son:

1. Pulsación en el segundo espacio intercostal izquierdo. Por un período de tiempo variable después de la obstrucción masiva de la arteria pulmonar, pulsaciones activas en el segundo espacio intercostal izquierdo pueden ser palpadas; puede hallarse también aumento sordo a la percusión sobre la arteria.

2. Un aumento en el segundo sonido pulmonar, más fuerte que el segundo sonido aórtico. Se oye un aumento marcadamente accentuado del segundo sonido pulmonar; en las fases tempranas de la embolia pulmonar masiva no existen estertores a excepción de los que ocurren como consecuencia de infartos previos, siendo estos últimos unilaterales.

3. Frotamiento pleuropericárdico o seudopericárdico. Un ruido de frotamiento pericárdico el cual tiende a localizarse en la parte alta izquierda del pecho en la región del segundo y tercer espacio intercostal puede causar confusión en la diferenciación entre el infarto del miocardio y la embolia pulmonar a menos que se sepa que el mismo puede ocurrir en la embolia pulmonar masiva.

4. Un soplo sistólico en el segundo espacio intercostal. Un soplo sistólico acompañado por un estremecimiento en el área pulmonar puede ocurrir como resultado de la oclusión parcial de la arteria pulmonar debido a un émbolo.

5. Un soplo diastólico en el segundo y tercer espacio intercostal. Este signo de embolia pulmonar sólo ha sido reportado dos veces en la literatura.

6. Un ruido en el área interescapular. Este signo más bien raro

ha sido atribuído a un trombo corredizo en la bifurcación de la arteria pulmonar.

7. Un rezagamiento en la expansión (unilateral). La expansión disminuida y el ruido respiratorio reducido cuando un émbolo obstruye la rama izquierda o derecha de la arteria pulmonar han sido observados.

8. Aumento de la percusión sorda cardíaca hacia la derecha. Cuando el corazón derecho falla en la embolia pulmonar masiva, el descubrimiento en el aumento de la percusión cardíada hacia la derecha del esternón es un signo físico importante.

9. Distención de las venas del cuello. La distención de las venas del cuello es una evidencia importante de fallo cardíaco derecho; la misma aumenta con la presión sobre el hígado.

10. Ritmo de galope en el segundo y tercer espacio intercostal. Es muy probable que el ritmo de galope ocurra con la obstrucción de la arteria pulmonar o de sus ramas principales.

11. Hepatomegalia. Cuando el fallo cardíaco derecho ocurre, el hígado puede estar doloroso y agrandado.

12. La "ondulación de sangre roja". Mientras observaba un paciente muriendo de embolia pulmonar masiva, Kirschner notó que una "ondulación de sangre roja" pasaba violentamente sobre la cara cianótica y pálida del enfermo por sólo breve tiempo. Un rato más tarde el mismo fenómeno aparecía por segunda vez. La explicación dada es que un fragmento del émbolo se desprende temporalmente permitiendo el pase de una cantidad adicional de sangre pura oxigenada a través del pulmón izquierdo, de donde es bombeada a la cara del paciente.

No es de esperarse que todos los pacientes muestren todos los signos enumerados, ya que el tamaño del émbolo, su localización y el grado de obstrucción que produce varían. Un émbolo grande en espiral que bloquee la arteria pulmonar o sus ramas principales puede ocasionar anoxemia del cerebro o del miocardio en un tiempo notablemente corto. Sin embargo, 51 por ciento de los pacientes con embolia pulmonar masiva han vivido más de quince minutos —tiempo adecuado para examinar por los signos descritos.

Muy a menudo, el émbolo pulmonar no es suficientemente grande para causar elevación marcada de la presión pulmonar, cuando así sucede tanto las manifestaciones clínicas como radiológicas pueden estar ausentes. Cuando los síntomas ocurren los mismos son el resultado del infarto asociado. El dolor tiene un carácter pleurítico típico y es de comienzo violento, hay alteración local en los ruidos respiratorios, estertores, tos, hemoptisis, y fiebre. Este cuadro clínico se asemeja estrechamente con el de una pulmonía lobar. En ambas condiciones la aceleración del ritmo respiratorio es des-

proporcionado cuando se lo relaciona con la fiebre y la taquicardia. El líquido pleural que ocurre a menudo es frecuentemente sanguinolento pudiendo ser confundido con efusiones debido a malignidad o tuberculosis.

Cuando hay embolias pequeñas recurrentes y las mismas producen pequeños infartos, el cuadro entonces puede simular el de una bronco-pulmonía, carcinomatosis pulmonar o enfermedades progresivas parenquimatosas. Tales pacientes pueden presentarse con disnea progresiva, con tos y fiebre irregular, estando ausentes la hemoptisis como el dolor pleural. Sin embargo, el diagnóstico se facilita cuando el dolor típico pleurítico está presente y asociado con frotamiento y dolor local. En cualquier paciente con evidencia de hipertensión pulmonar reciente, una radiografía de pecho negativa no excluye la embolia pulmonar múltiple como la causa.

Los episodios de embolización pulmonar repetidos pueden producir aterosclerosis pulmonar. La embolia puede interferir con el flujo sanguíneo, aumentando la tensión de la arteria pulmonar produciendo el Corazón Pulmonar y fallo cardíaco. La hipertensión acentúa y acelera el desarrollo de enfermedad en la íntima, lo mismo que en las arterias sistémicas. Los vasos en la parte inferior de los pulmones son los más severamente afectados. Con el desarrollo de la oclusión, un aumento proporcional del flujo sanguíneo pulmonar es desviado a canales menos afectados o no afectados, los cuales sufren entonces la secuencia de cambios descritos en las formas hiperquinéticas de la hipertensión pulmonar. Los cambios más notorios ocurren en las arteriolas y las pequeñas arterias musculares (1 mm. o menos). El vasoespasmo es seguido por hiperтроfia de la musculatura media, con engrosamiento fibroelástico de la íntima o fibrosis final produciendo estrechamiento u obliteración del lumen arterial. De suerte que la hipertensión pulmonar que se asocia con el tromboembolismo pulmonar crónico es del tipo "obstructivo". Es la resultante de fenómenos primariamente mecánicos con una pérdida significativa pulmonar vascular y un aumento en la resistencia de la misma. La reducción vascular sin embargo, debe exceder alrededor de dos tercios del total antes de que la hipertensión durante el descanso ocurra. El sondeo cardíaco revelará entonces una elevación de la presión de la arteria pulmonar y del ventrículo derecho al igual que en el atrio derecho y las venas sistémicas. La presión pulmonar capilar venosa (presión "cuña") no se eleva, pero es a menudo imposible avanzar el cateter que choca contra el émbolo o se arrolla en un corazón derecho dilatado. Una disminución durante el descanso del vaciado cardíaco, y/o una respuesta inadecuada al ejercicio en relación al consumo de oxígeno es usualmente observado.

El fracaso en la indentificación de la hipertensión pulmonar tromboembólica conduce al diagnóstico erróneo de hipertensión pulmonar primaria.

**DIAGNOSTICO.** El reconocimiento del infarto pulmonar depende principalmente, de la combinación de un índice alto de sospechas, con exámenes cuidadosos repetidos de las piernas para evidenciar la enfermedad venosa trombótica. La enfermedad usualmente ocurre en pacientes con desórdenes que predisponen a la flebotrombosis. Siendo así es frecuente en pacientes con policitemia, fallo cardíaco congestivo, durante los períodos del post-operatorio y del post-parto o en personas de edad avanzada quienes están postrado en cama por cualquier razón. No es raro en individuos aparentemente saludables siguiendo viajes largos en aviones o automóviles asociados con inmovilidad y dependencia de las piernas. En cualquiera de tales personas, la ocurrencia de dolor pleural, disnea violenta, hemoptisis, sícope o efusión pleural sanguinolenta la sospecha de infarto pulmonar está en orden.

El fallo cardíaco congestivo es la más común de las varias condiciones predisponentes. En ausencia de la terapia anticoagulante, alrededor del 60 por ciento de los pacientes con estenosis mitral y 40 por ciento de los individuos muriendo de fallo cardíaco congestivo debido a otras causas demuestran en la autopsia haber tenido uno o más infartos pulmonares. La única pista clínica en estos pacientes puede ser un empeoramiento violento en el estado clínico, con aumento en la disnea, y contumacia a la terapia, acompañado de elevación temporera del contejo leucocitario y sedimentación de los glóbulos rojos. Ocasionalmente ocurre ligera ictericia y es debido no al aumento en la destrucción de eritrocitos sino más bien al deterioro súbito en la función hepática debido a la congestión creciente como resultado del aumento de la presión pulmonar. Aunque el examen diario de las piernas a menudo muestran algunos signos de trombosis venosa, estos fenómenos pueden hallarse completamente ausentes, a pesar de la exploración más cuidadosa.

Los signos radiológicos directamente atribuibles a la Embolia Aguda Pulmonar no son ni notables ni tampoco específicos. Las sombras hiliares y las marcas pulmonares vasculares pueden hallarse más dilatadas de lo normal. El ángulo medio izquierdo puede estar prominente debido a la dilatación de la arteria pulmonar. Los estudios radiológicos pueden sugerir la presencia del infarto pulmonar resultante de la embolia. Las sombras de los infartos pulmonares pueden no aparecer hasta veinticuatro horas o varios días después de que la embolia pulmonar ocurre. Un signo temprano del infarto pulmonar, de acuerdo con Wharton y Pierson, es el obscurcimiento de la base del pulmón, ocultando el seno costofrénico

del lado afectado. Los infartos son a menudo múltiples y ocurren principalmente en los lúbulos inferiores. Las sombras de los infartos pueden tener la forma clásica triangular pero con más frecuencia son irregulares, redondas u ovaladas. A menudo son indistinguibles de infiltraciones pneumónicas o de congestión pulmonar severa debido al fallo cardíaco. De acuerdo con Hampton y Castleman, los infartos pulmonares ocurren más amenudo en la unión de dos superficies pleurales y por lo tanto las sombras radiológicas son observadas en las bases de los pulmones, cerca del surco costofrénico, en la unión de lóbulos contiguos y cerca del mediastino. Las efusiones pleurales son frecuentes y las mismas pueden ocultar la sombra del infarto. Podría encontrarse una sombra en una de las bases con elevación del diafragma del mismo lado, debido a la atelectasia parcial. Con rareza hay rarefacción localizada, indicando absceso o necrosis. Espesamiento pleural, fibrosis localizada o sombras lineares pueden representar cicatrices de infartos viejos. De acuerdo con Westermark y otros, la embolia pulmonar sin infarto puede causar un aclaramiento transitorio (avascularidad) de la sombra normal de tejido pulmonar distante de la embolia.

En un estudio reciente por Sasahara, y colaboradores se hace énfasis de la angiografía pulmonar como medio de diagnóstico de la enfermedad tromboembólica pulmonar y la utilidad de la misma cuando los hallazgos físicos son escasos y la historia médica obscura. Estudiaron estos autores once pacientes en los cuales se sospechaba el diagnóstico de Embolia Pulmonar. En ocho de ellos el diagnóstico se comprobó mediante este procedimiento. En dicho estudio se recalca la utilidad de la determinación de la dehidrogenasa láctica sérica. En cuatro pacientes en que la misma se determinó estuvo consistentemente elevada mientras que la transamínsa glutámica oxalacética permaneció normal.

**TRATAMIENTO.** El tratamiento se divide en tres partes: 1. Impedir la formación de coágulos en las venas de las piernas mediante la ambulación temprana o mediante el vendaje de las extremidades inferiores cuando el paciente está confinado en cama, también mediante el uso de los anticoagulantes. 2. Prevenir la embolia pulmonar una vez las piernas están comprometidas. La terapia con anticoagulantes es usualmente satisfactoria. Ocasionalmente en algunos pacientes las embolias pulmonares continúan a pesar de los anticoagulantes. En tales casos la ligadura de ambas venas femorales o de la vena cava se hace necesario. 3. Evitar la destrucción de las venas y vasos linfáticos lo que conduce a úlceras crónicas y edema persistente. El dolor es aliviado y el edema disminuye más rápidamente cuando el tono simpático es liberado mediante el bloqueo paravertebral. La terapia con anticoagulantes puede reducir

el número de vasos permanentemente trombosados. La elevación de la pierna al igual que el vendaje reducen el edema. Una atención particular debería dársele al vendaje cuando al paciente le es permitido levantarse.

La hemoptisis, a menos que sea masiva no constituye una contraindicación para el uso de la terapia con anticoagulantes. En la mayoría de los casos, los anticoagulantes prevendrán las recurrencias. Si ésto no sucediera entonces sería necesario ligar ambas venas femorales o bien la vena cava inferior debido a que aunque exista evidencia de tromboflebitis o flebotrombosis en una pierna ello no implica que las embolias tengan su origen en el lado opuesto. Frecuentemente proceden de la extremidad opuesta, a menudo silenciosa. Existe alguna evidencia de que el aumento en la resistencia vascular pulmonar que sigue a la embolia es debido, al menos en parte, a la liberación de serotonina del coágulo sanguíneo y que la heparina tiende a neutralizar este efecto. Por lo tanto, la heparina es preferible a otros anticoagulantes durante la fase inicial del tratamiento. Se administra en dosis de 50 a 75 mg. por vía intravenosa cada 6 a 8 horas, o con una pequeña cantidad de procaína por vía subcutánea. El gasto y la inconveniencia de tantas inyecciones usualmente induce al médico a usar uno de los derivados de la cumadina después de los primeros 2 o 3 días.

**PREVENCION.** Las condiciones que predisponen al estancamiento venoso deberían combatirse. Los pacientes predispuestos deberían usar medias elásticas y, en ausencia de contraindicaciones apremiantes, caminar por algunos minutos varias veces al día es aconsejable. Cuando ésto es indeseable, el masaje a las pantorrillas con movimientos activos o pasivos de las piernas debiera ser instituído a cada pocas horas. Es altamente probable que estas medidas reduzcan la frecuencia de la flebotrombosis.

**PRONOSTICO.** Las probabilidades de supervivencia después de una embolia pulmonar masiva son extremadamente desfavorables. Cuando la embolia es suficientemente grande y ocasiona "shock" o dilatación ventricular derecha, la muerte ocurre en la mayoría de los casos. De 100 pacientes de embolia pulmonar reportados por Takats, Beck y Fenn, 87 murieron y 37 sobrevivieron. Igualmente Hampton y Wharton reportaron una supervivencia de 10 por ciento en pacientes con embolia pulmonar después de operaciones ginecológicas. La embolia pulmonar es considerada como responsable en alrededor de 6 a 10 por ciento de todas las muertes en los estados post-operatorios. La embolia pulmonar en las ramas secundarias o más pequeñas tiene generalmente un mejor pronóstico pero frecuentemente precursan recurrencia que pueden terminar con una embolia masiva de la arteria pulmonar o de sus divisiones

principales. En 24.4 por ciento de 897 casos de embolia pulmonar estudiados por Baker, y colaboradores el ataque inicial fué fatal. Pero de 343 casos mortales de embolia, la embolia letal fué precedida por una o más embolias no mortales en 36.2 por ciento. Estos observadores hacen notar que si un paciente tiene una embolia pulmonar no-fatal en el estado post-operatorio dicho paciente tiene ligeramente menos de una oportunidad en cinco de embolia pulmonar fatal subsiguiente y alrededor de tres oportunidades en diez de embolia subsiguiente no-mortal o mortal. Los síntomas y signos clínicos de la embolia pulmonar pequeña usualmente desaparecen en una o dos semanas pero el curso clínico pudiera prolongarse debido a efusión pleural o a supuración del infarto.

En raras ocasiones una embolia pulmonar de las arterias primarias pulmonares podría no causar la muerte pudiendo pasar por un período de organización y recanalización. Tanto en este último tipo de embolia como en las embolias pequeñas recurrentes pueden ocasionalmente producir hipertensión pulmonar, hipertrofia ventricular derecha y fallo cardíaco (Corazón pulmonar crónico).

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## THE SEXUAL SYNDROMES

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### Remarks on Classification

It is indeed strange that to address you should be in any way unusual. As a group of professionals, you deal, in physical actuality, with the very same organs whose mental representation has become the core of psychiatric practice since the advent of Sigmund Freud and his theories. It is appalling to realize how far apart we have been as colleagues and how seldom we have the opportunity of getting together. It was through the kind invitation of your President that this opportunity was presented and I grabbed it immediately.

As a matter of introduction, let me draw from my practice to illustrate in a festinate case, the disparity between the conceptual or mental representation of the organs in question and their physical reality.

Be aware that I have still to call them sexual, urinary, or reproductive organs and each of us, depending upon our approach, will probably name them differently.

We are all familiar with the condition of criptorquidea, its treatment, evaluation, and its incidence.

Some time ago, a 27-year-old patient of mine, who underwent psychoanalytic treatment for a condition of difficulty in heterosexual adjustment, brought the following dream to a session. "It was night time — I was walking in the street — authorities were asking for some kind of identification card — I was asked to present my card — and could not find it in my wallet — I went back home where I found it amongst a key chain, a white handkerchief and a ten-dollar-bill." We worked the dream, through associations, that walking the streets at night is a male prerogative which his parents kept him from gratifying far into his adulthood; the card represented a selective service card, which is a sign of maleness; the key is a very frequent phallic symbol; the handkerchief reminded him of a handkerchief he had at home with a few mementoes from his one and only romantic involvement with a girl, and this needs no explanation in relation to the theme of the dream.

We kept asking for associations to the ten-dollar-bill and, every time, we ran against a blank wall except that the patient went on explaining that what came to his mind was the number

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ten, as it appeared in the bill. In the next interview, and to our surprise, the patient started talking about an experience he had when he was 11 years old, in which he remembered clearly that he had been taken to the family physician who prescribed some injections. Upon questioning, he remembered further, that the examination included an examination of his testicles. It was only under close scrutiny that he kept adding information long since forgotten. The injections had been prescribed because, somehow, he had only one testicle. This one testicle, with his penis, became the ten in the bill that we could not understand at the beginning.

Getting closer to our theme, I want to explain why I choose to talk about syndromes. They are a combination of symptoms that are usually the facade of underlying pathology, and there is very little done to systematize their study in the literature. In most nomenclatures, they are dealt with under the heading of "Psychoneurosis Associated With" — and, then, one of the difficult names is stated. Others put all the sexual difficulties under a general heading of "Social and Sexual Maladjustments". Even at the start, we may have some confusion with the very use of the word "sexual". In some literature, the word "sexual" is used as tantamount in meaning to pleasure, equating every pleasure with sexuality. For this paper, I equate sexual with orgasmic and thus consider coition, or cohabitation, the matrix of orgasmic behavior. Centrally, we will be dealing with a standard coital pattern.

In dealing with the sexual syndromes, we have to start by stating a number of tenets. How much is biologically determined and how much is culturally tinged, or learned, in sexual behavior? We find out that very little is biologically determined. Sexual behavior is learned behaviour and thus modifiable by experience and by therapy. The biologically determined parts of sexual behavior are: 1—Erection in the male with the concomitant pelvic thrust and lubricity in the female, and 2—Orgasm. These are the only parts that can respond in a simple reflex arc.

It is apparent from the experiments done on higher primates, that if two healthy human beings could be raised with no knowledge of the sexual differences and were put together as adults, they would simply not know how to proceed or what to do. So, we repeat ourselves. Sexual behavior is learned behavior.

As a learned and developed behavior, there are social and cultural factors in sexual behavior and, thus, any classification of its malfunctions has to take into consideration the changes in the social and cultural mores.

We cannot talk of one sex but of two sexes, and they only exist in relation to each other. As stated by Professor Sandor

Rado, "there are males, there are females, and there are cripples". The concept of bisexuality, or hermaphroditism, has been instrumental in confusing this whole subject and must be evaluated properly. We see the copulatory apparatus as a biological continuation of the egg and sperm which seek to unite. The whole individual is the bearer of both germ cells and a copulatory apparatus, who comes to understand that he is the bearer of such potentials. We have to look with great doubts at all the far-reaching, sweeping statements which are a result of the observation of animal behavior and that, by extrapolation, are later applied to human behavior. In dealing with the question of the motivation of sexual behavior, we find that in man, we have direct, investigative access to the dynamic level through which the motivation of behavior can be explored and explained in verbal, descriptive terms. The cultural pattern which surrounds him serves as a framework.

Man is born with responses constituting his mammalian heritage, into a web of social institutions which control and determine his behavior from birth to death. There ensues a degree of variability unknown to other species. In man, we see that coition is dominated by the desire for orgasmic pleasure. This hedonic motivation is independent of reproductive intent which may be combined with it or not. Orgasm, an intermediary phase in reproduction, is the final goal in this hedonic pursuit.

In order to apply a classification of syndromes, we have to try to define the function. To avoid difficulties inherent in the subject, we shall try first, to describe normal sexual functioning or the standard coital pattern. This is a derivation from the physiological concept of a reproductive pair to the psychodynamic concept of an orgasmic pleasure pair. Moreover, the orgasmic pleasure scheme is considerably enlarged through contributions derived from extra-genital sources.

First, let us consider the cultural milieu. With very slight changes as far as sex is concerned, we are still living under the same influences as Victorian society with the value it attached to virginity in the females, its prevalent double standards, and the market value of low or high marriage possibilities. The strides achieved by science in the conquering of venereal diseases, and the improvement of contraceptive methods are too new to have had any impact upon sexual behavior as a collective phenomenon.

In the standard coital pattern, internal stimulation establishes receptivity to psychological stimulation; arousal can be sensory, visual, tactile, etc., or intellectual, whether by reading poetry, talking, looking at paintings, dancing the "Twist", or listening to Bach or to Bartok. In both mates, this sets up a sexual motive state

which mobilizes and organizes all the sources for orgasmic pleasure. In both mates, this elicits automatic responses of preparedness: at a sensory level, mechanisms of selective attention; at an intellectual level, selective mechanisms of memory and wishful thought; at a motor level, engorgement and erection of erectile structures; at a glandular level, secretion of vehicular and lubricating fluids.

Wooing and securing consent follows foreplay, with mutual stimulation of responsive extragenital regions.

A rising of impetus to penetrate, in the male, is attended by the rising of the desire to be penetrated, in the female. In play, orgasm, heightened pride, and desire to sleep complete our concept of the standard coital pattern.

The impact of early fears, rages, and threats can impinge upon any of these stages and paralyze the individual. We have even more to consider than what has just been stated, because thus far in the standard coital pattern, no mention has been made of the socio-cultural level at which it occurs. To this standard coital pattern, we have to add such variables as the concepts of sensual love, magic love, the in-love pair, interest in security, desire for offspring, marriage, and the pride and sense of status these might afford. You may find a person who can follow all the stages of the standard coital pattern and who still is unable to engage in a more or less permanent relationship. He or she keeps breaking engagements, interested only in partners that do not represent marital prospects, etc., and this pattern can lead to a very unhappy and sick situation.

In the exploring of this syndromes, we have to be aware, also, that inspection, palpation, etc., as medical methods of examination have to give way to careful interrogation and, more than that, to careful listening.

From this enlarged physio—, psycho-cultural concept of the standard coital pattern, we can now make first attempt at classification or division, namely: I. ANTISEXUAL BEHAVIOR, II. Disturbance in the execution of the standard sexual pattern.

I. Antisexual behavior involves complete and longlasting repression or suppression of sexual thoughts, activities, or desires with hostility to and separation from any sexual situation. It includes a lack of sexual dreams, phantasies, and masturbation. This diagnosis conveys evidence of a deep-seated, serious difficulty in the realm of schizophrenic disintegration. In the female, this diagnosis should be made only with great care because, from a social point of view, antisexuality in the female can be very misleading. Antisexuality can be confused with an extension of frigidity. It is interesting to notice that in the female in Puerto

Rico, we sometimes see pseudo-antisexual behavior, even in non-frigid females. Antisexuality has also to be distinguished from sexual abstinence and sexual incapacity.

**II. Disturbances in the execution of the normal pattern** have to be divided into disturbances in the male and disturbances in the female.

The disturbances in the male, sex failure in the presence of desire distinguishes these from the above-mentioned antisexual syndrome. When seen on consultation, there have already been repeated failures, despite desire, which are embarrassing, humiliating experiences that lower the self-esteem of the individual and that have to be probed with great care. Any tinge of irony or accusation in the voice of the examining physician can be fatal. The type of failure can be subdivided into; 1—Desire and total lack of erection; 2—Desire and partial erection; 3—Loss of erection at intent of penetration; 4—Ejeculatio anteportas, which is ejeculatio at intent of penetration; 5—Ejeculatio praecox, and 6—Ejeculatio retardata.

Any of these subdivisions has to be weighed in the light of chronicity, or the response of the patient to the condition, and response of the partner, in order to establish prognostic and therapeutic criteria. Just to illustrate the amount of confusion in this field, such an important, serious, and valuable study as **The Kinsey Report on Sexual Behavior** brushes aside the idea of ejeculatio praecox. Even Kinsey declares as normal, any coital pattern that ends in ejeculatio in the vagina without consideration of the time of intramural play.

These disturbances of the male pattern are the result of long-range, retrospective experiences in which penetration is equated with murder or assault. For a child, the observation or overhearing of an adult couple in sexual intercourse can be easily misinterpreted as murder. These are irrational fears and, as such, have to be understood.

To show how irrational these fears are, let me give you an example. A patient may be unable to have intercourse because he may envisage the vagina as full of teeth that would bite his penis away and, at the same time, may have, as his sole sexual outlet, a mouth-genital pattern, and in a mouth which really has teeth he can have ejaculation. He fades away from the vagina because he unconsciously believes it has teeth and substitutes for it, a mouth that he is conscious has teeth.

Disturbances in the female pattern consist of complete vaginal anesthesia (frigidity). If it is not the result of the antisexual syndrome, this condition can be total or partial. Responsiveness to stimulation of other erogenous zones may be present or absent.

There may be responsiveness of clitoridial at stimulation or perianal zones. As its counterpart in the male, the condition can be subdivided into pre-penetration, on-penetration, and post-penetration and can be accompanied by a lack of secretion of the usual lubricating fluids. Cases of dyspaneuria should first be evaluated from the physical point of view.

Again, we are in the presence of unconscious fears, as in impotence. Frigidity has to be evaluated as to chronicity, continuity, and response. In treatment of both conditions of male and female, the unavailability of an understanding and industrious partner is very desirable, as an ironic, castrating partner can easily destroy weeks of therapy. These fears may paralyze the individual at various stages in the process and can include, besides the actual sexual situations, social and professional situations that are unconsciously linked with sex.

III. The modified patterns. In the modified patterns of sexual behavior, no penetration of the male organ occurs; orgasmic peristalsis of genital structures (orgasm), is elicited by other kinds of stimulation.

Although the criterion of motor behavior would suffice to differentiate the standard from the modified patterns, we must also examine underlying motivations and mechanisms which prove of extreme importance. In the clinical material, the modified patterns could be subdivided and have to be evaluated as **Reparative**, if they are ushered in by the inhibition or incapacity for standard performance, or **Situational**, if it is because of lack of opportunity, segregation, or other circumstances that may force even the healthy individual to seek orgasmic satisfaction by temporarily adapting, through conscious deliberation, a modified pattern, or **Variational** in which some individuals, under ordinary circumstances, yield to a desire for variations of performance.

The Reparative patterns may be classified as follows: Organ avoidance and organ replacement.

To avoid the genital organ of the opposite sex, the individual may go through painstaking procedures, most of which appear unintelligible on observation. The organ, the whole individual, or the situation is avoided because of fears. These are unconscious fears of castration or fears of penetration. The avoidance may be of the organ only, or of the whole person, or of the whole situation. Sometimes it takes the form of avoidance of sex with a particular person, usually the wife or husband. At other times, it takes the form of procrastinating and perpetually postponing. It may be disguised by bouts of drinking, getting home late, prolonged toilet care before bed so that the partner will be already asleep,

tiring oneself enough so as to drop into exhausted sleep, prolonged reading or TV viewing, etc., etc.

Avoidance is accompanied by a process of replacement or substitution with an intent at reparation. The dreaded organ may be replaced by another part of the body of the partner; e.g., mouth-genital contacts, anus-genital, mutual masturbation, or intercourse interfemora. The reparative patterns often evolve from a form of arousal discovered and practiced in the early years of development. Avoidance sometimes takes the form of avoiding the adult sexual organ and the pattern may take the criminal form of pedophilia or sex acts with children.

Sometimes the avoidance is so all-pervasive that it becomes total and amounts to almost solitary gratification, using the mate solely as an object of contemplation. This includes the exhibitionist who is capable of achieving orgasm only by abrupt exposition and manipulation of his sex organs, and the voyeur who advances to orgastic satisfaction by spying on a woman's sexual privacy.

The avoidance of the adult sexual organ can also take the form of human-animal pairs, or zoophilia erotica to use Kraft-Ebbing terminology.

#### **Patterns of Solitary Gratification.**

In this group, orgasm is achieved in the absence of the physical presence of a mate. Orgastic self-stimulation or masturbation, with a phantasy or daydream of an illusory twosome, can be regarded as a normal form of gratification during a certain period of development. When, in the absence of situational expedients, it becomes the only way in which the individual can achieve gratification, it has to be considered pathological.

Blanck orgastic self-stimulation or masturbation, in the absence of daydreams or phantasy, must be looked upon as very sick, probably the product of schizophrenic disintegration.

In surprise orgasm, wet dreams etc., have to be evaluated according to the situational expediency of other sexual outlets. Under normal circumstances, they should be explored as an organ avoidance syndrome.

In some cases, the mate can be "represented" as in the fetishist, by a characteristic possession of the beloved as a sexual object. It can be a shoe, a piece of hair, a garment.

Transvestitism is the sexually-significant wearing of clothes of the opposite sex. It is used in the process of self-stimulation or masturbation.

#### **Patterns of Sexual Pain-Dependence.**

These have become popular and over-dramatized in the clinical description of Von Kraft-Ebbing who named them sadism and

masochism, after the description of the French Marquis de Sade and an Austrian novelist, Sacher Masoch.

Sexual pain-dependence may appear in (1) criminal, (2) dramatized, or (3) hidden forms. In the criminal manifestations, it precipitates what amounts to a savage execution of the sexual act as a concept of violence. These include lust murders and concomitant ejaculation in wounds, necrophilia or sex with cadavers.

In sado-masochistic practices, two consenting mates inflict pain short of severe and serious physical injury upon each other in a dramatized version of the violent conception of the sexual act.

The hidden forms of sexual pain-dependence, by far more important clinically, are extremely common. They are revealed in a large variety of clinical manifestations: quarreling as a prelude to a truly happy embrace, use of torturing, irrational jealousies as an aphrodisiac, etc.

#### **Homogeneous Pair or Homosexuality.**

In homosexuality, the divisions are in male and female pairs. Individuals, deterred by fears and resentment from the opposite sex, may find orgastic satisfaction with a mate of the same sex. Male pairs are based on the reassuring presence of the male sexual organ, and female pairs are based on the reassuring absence of the male sexual organ.

At a popular level, a large distinction is made in delineating passive or recipient homosexuality versus active homosexuality. From a clinical point of view, this difference is not of great help and I would advise, instead, that cases be evaluated more in terms of duration, variability of the pattern, and age. A distinction can be made between poly- and mono-homosexuality in both male and female; that is, patients who practice the act with various partners and those who practice it with only one. In many cases, although there is short-lived sexual behaviour among the partners, most of the behaviour is nonsexual. It belongs, again, to the organ avoidance syndrome and some of these patients are better termed homo-social rather than homo-sexuals. One aspect that is very seldom pointed out is that homogenous pairs tend to imitate the long-established, male-female couple and usually become a caricature of heterosexual couples, one imitating the male and the other imitating the female.

Patterns involving more than two mates are usually a derivation from the original orgies, and may include such criminal actions as rape done by a group with a changing of partners. Under some of these conditions, sexual arousal is increased by the unconscious security obtained from the presence of multiple, male sexual organs.

**THE SEXUAL SYNDROMES**From: Prof. Sandor Rado  
Psychoanalysis of BehaviorGrune & Stratton, 1956  
(Modified)**THE STANDARD COITAL PATTERN***Internal Stimulation**Sensual Motive State**Preparedness*Sensory  
IntellectualMotor  
GlandularWooing  
ForeplayImpetus to ----- Penetrate  
Be Penetrated

Inplay

Orgasm

Sensual Love

Magical Love

In Love

Interest in Security

Desire for Offspring

Marriaga

Pride

**I— ANTI-SEXUAL BEHAVIOR****II—DISTURBANCES IN THE EXECUTION OF THE STANDARD SEXUAL PATTERN***A— In the Male*

- 1— Desire with total lack of erection (impotence)
- 2— Desire with partial erection

*B— In the Female*

- Vaginal anesthesia (frigidity)
- 3— Loss of erection at intent of penetration
- 4— Ejaculatio antepora
- 5— Ejaculatio praecox
- 6— Ejaculatio retardata

**III—MODIFIED PATTERNS:**  
(can be reparative, situational or variational)*A— Organ Avoidance and Replacement*

- 1— Mutual masturbation, mouth-genital anus genital, etc.
- 2— Exhibitionism, voyeurism

*B— Patterns of Solitary Gratification*

- 3— Adult-child pairs
- 4— Masturbation (in the blanck)
- 5— Homogeneous pairs (homosexuality)

*C— Patterns of Sexual Pain-Dependence*

- 1— Sadism
- 2— Masochism
- 3— Hidden sexual Pain-dependency

*D— Patterns involving more than two mates (Plurality)*

- 1— Feticism
- 2— Transvestitism
- 3— Masturbation (with phantasy or day dreams)
- 4— Masturbation (in the blanck)
- 5— Wet dreams

The use of drugs, although it may change the sexual pattern occasionally, is never long-lasting and even the use of alcohol, which initiates disinhibitory behavior with a feeling of increasing capacity, ends with the opposite becoming true. As its intake continues, there is less and less capability for performance and the alcohol becomes a substitute.

To finish my comments. There is much that can be done to alleviate the suffering implicit in these conditions. In some of short duration, a sympathetic ear and reassuring voice are helpful. In others, prolonged, continuous, and painstaking psychoanalytic procedures are needed.

I want to make a special distinction about antisexual behavior, polymorphous aberrant patterns of sexual behavior, and sexual patterns of schizophrenic patients which must be understood, not as variants of the standard patterns, but as the expression of very strange thought and emotional processes.

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## SECCION DE RESUMENES

**ALLERGIC DISEASES IN ADOLESCENTS. II. CHANGES IN ALLERGIC MANIFESTATIONS DURING ADOLESCENCE.** (Enfermedades alérgicas en adolescentes. II. Cambios en sus manifestaciones durante la adolescencia.) Freeman, G. L. and Johnson, S., University of Colorado Medical Center. *A M A J. Diseases of Children* 107:549 (June) 1964.

Se ha informado que en la mayoría de los niños el asma desaparece durante la adolescencia, pero no se conoce la razón por la cual esto ocurre y se ha asumido que otras manifestaciones alérgicas siguen el mismo patrón. El estudio es una continuación de una encuesta entre estudiantes de las escuelas públicas de Denver. Incluye 2,627 niños de octavo y décimosegundo grado, de los cuales 431 tenían o habían tenido manifestaciones alérgicas. Se encontró que mientras más joven el paciente era cuando desarrollaba los primeros síntomas alérgicos, más probabilidades tenía de tener manifestaciones alérgicas múltiples. En el 25% de los casos de asma, ésta había desaparecido a los 10 años. El mejor pronóstico se encontró cuando el asma empezó antes de la adolescencia. Entre los niños cuyos ataques de asma empezaron antes de los 10 años, ésta desapareció o mejoró durante la adolescencia en el 82%, mientras que esto ocurrió en solamente el 53% de los estudiantes entre quienes el asma comenzó durante la adolescencia. La edad promedio en que el asma desapareció en la mayoría fue de 11 años en niñas y 13 años en varones. Muy pocos casos mejoraron después de los 13 años en ambos sexos. Otras manifestaciones alérgicas como rinitis alérgica, dermatitis atópica y urticaria, en contraste con el asma, raras veces desaparecieron durante la adolescencia. Los autores no han encontrado una explicación adecuada del porqué existe esta diferencia entre el asma y otras manifestaciones alérgicas, ni creen que haya una explicación hormonal que explique la desaparición del asma en los adolescentes. Advierten que aunque el asma tenga buen pronóstico en la adolescencia los niños asmáticos deben recibir tratamiento adecuado, para evitar daño broncopulmonar y síquico permanentes.

J. E. SIFONTES, M. D.

**DIAGNOSIS AND TREATMENT: MANAGEMENT OF IDIOPATHIC THROMBOCYTOPENIC PURPURA.** (Diagnóstico y tratamiento de púrpura idiopática trombopénica). Schulman, I. Department of Pediatrics, University of Illinois, College of Medicine, Chicago, Ill. *Pediatrics* 33:979, (June) 1964.

Púrpura trombopénica idiopática se caracteriza por un conteo de plaquetas menor de 50,000, médula ósea normal o con aumento de megacariocitos y ausencia de enfermedad sistémica o ingestión de drogas causantes de púrpura. Leucemia y Lupus deben descartarse. Sin tratamiento el pronóstico es excelente en el 80% de los casos. Tres cuartas partes mejoran dentro de un período de tres meses. Un 20%, designados como crónicos, continúan enfermos por más de 6 meses. La mortalidad es baja y el problema de mayor urgencia es hemorragia en el sistema nervioso central, la que ocurre en alrededor de un 2 a 4% de los casos. Por lo general todas las manifestaciones hemorrágicas graves ocurren en los primeros días de la enfermedad. Se cree que, no solamente son debidas a la disminución en plaquetas, sino a anomalías de los pequeños vasos sanguíneos. Los corticosteroides se usan para disminuir el peligro de grandes hemorragias pero no mejoran el pronóstico final en cuanto a la cronicidad de la enfermedad y si se continúan por tiempo prolongado

pueden suprimir la formación de plaquetas. Se recomienda el tratamiento con prednisona en dosis de 1 mg./kg. de peso/tres semanas y disminución gradual hasta interrumpirlo durante la cuarta semana del tratamiento. No debe continuarse el tratamiento con esteroides aún cuando las plaquetas continúen disminuidas. Si la trombopenia persiste más allá de tres meses de enfermedad se puede repetir el curso de esteroides por otras cuatro semanas. Si la trombopenia persiste por más de 6 meses debe considerarse la esplenectomía. Generalmente esta se hace si la enfermedad persiste más allá de un año. Los resultados de la operación son favorables en las dos terceras partes de los casos. En algunos niños con síntomas mínimos puede esperarse más tiempo antes de hacer la esplenectomía. Son raras las infecciones graves como resultado de esplenectomía por púrpura trombopénica idiopática.

El uso de transfusiones de plaquetas y sangre fresca para controlar la hemorragia durante la fase aguda es raras veces necesario. Transfusiones de plasma para estimular la trombopoyesis se considera un tratamiento todavía en su fase experimental. Al resumir, apunta el autor que debe tratarse el paciente y no el contaje de plaquetas.

J. E. SIFONTES, M. D.

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**HISTOPLASMOSIS IN CHILDREN. (Histoplasmosis en niños), Tesch, R. B., Shacklette, F. H., Diercks, D. H. and Hirschl, D. Del Hospital Gorgas, Zona del Canal de Panamá. Pediatrics 33:894, June 1964.**

Los autores opinan que histoplasmosis es una enfermedad común, benigna que pasa desapercibida en la mayoría de los casos. Informan 6 niños observados en Panamá con cuadros clínicos ilustrativos de las formas más severas de la enfermedad. El caso número 1 era una niña de cuatro años con un cuadro clínico parecido a tosferina complicada por bronconeumonía y fiebre inexplicable. Inicialmente las pruebas serológicas e intracutáneas para histoplasmosis eran negativas y el diagnóstico se hizo por cultivos del coágulo de una muestra de sangre. La enferma mejoró espontáneamente y las pruebas cutáneas y serológicas se tornaron fuertemente positivas durante la séptima y décimoprimeras semanas de enfermedad respectivamente. El caso número 2 era una niña de siete años con fiebre y hepatomegalia. El diagnóstico se hizo a base de biopsia de hígado y muestra de médula ósea en las que se encontró el Histoplasma capsulatum. Las pruebas cutáneas y serológicas fueron negativas en la primera semana de la enfermedad y positivas a los 30 días de la enfermedad. Se trató con sulfa por 3 meses y mejoró. El caso número 3 era una niña de 16 meses con fiebre, tos, infiltración en el lóbulo superior derecho del pulmón, adenopatía hilar derecha y tuberculina negativa. El diagnóstico se hizo a base de pruebas cutáneas y serológicas positivas, pero no se pudo aislar el hongo. Mejoró espontáneamente después de 20 días de enfermedad. El caso número 4 era un niño de un año de edad con fiebre, tos, diarrea y pérdida de peso desde los 10 meses de edad. Tenía anemia y hepatosplenomegalia moderadas. Inicialmente tuberculina, histoplasmina y pruebas serológicas fueron negativas. Radiografía de tórax demostró infiltraciones en ambos lóbulos superiores y en el lóbulo medio. El diagnóstico se hizo en el tercer mes de la enfermedad por cultivos positivos para histoplasma capsulatum de sangre y médula ósea. Las pruebas cutáneas y serológicas para histoplasmosis se tornaron fuertemente positivas después del octavo mes de enfermedad. El tratamiento fue sulfadiazina a niveles sanguíneos de 6 a 10 mg. por 100 cc, durante ocho meses. El enfermo mejoró aunque la hepatomegalia persistió. El caso número 5 era un niño de 5 años con fiebre, tos y disnea de origen

agudo. Fue tratado a principio como un caso de asma complicado por pulmonía. Pruebas serológicas y cutáneas para histoplasmosis eran negativas inicialmente, pero convirtieron a positivo a los 18 días de la enfermedad. No se cultivó el hongo. El caso número 6 era un niño de 6 años de edad con fiebre inexplicable e infiltraciones en el pulmón izquierdo. La prueba cutánea de histoplasmina fue positiva inicialmente y la prueba serológica negativa, pero ésta se tornó positiva durante la tercera semana de la enfermedad. El enfermo mejoró sin tratamiento específico. Al resumir, los autores apuntan la importancia de (1) los cultivos para hacer el diagnóstico, (2) la posibilidad de que el tratamiento con sulfa sea tan efectivo como el de anfotericin B y (3) no descartar el diagnóstico de histoplasmosis porque las pruebas cutáneas o serológicas sean inicialmente negativas.

J. E. SIFONTES, M. D.

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**CERVICAL ADENITIS IN CHILDREN DUE TO HUMAN AND UNCLASSIFIED MYCOBACTERIA. (Adenitis cervical en niños por Micobacterias humanas y no clasificadas), Black, B. G. and Chapman, J. S., University of Texas, Southwestern Medical School. Pediatrics 33:887, June 1964.**

Los autores estudiaron adenitis por Micobacterias en el Centro Médico de niños de Dallas, Texas, desde el 1956 hasta el 1962. Los estudios incluyeron biopsia, incisión y drenaje o aspiración con aguja, pruebas intracutáneas con antígenos derivados de grupos I, II y III de Micobacterias y tuberculina antigua. También se hicieron pruebas serológicas para Micobacterias y hongos como histoplasma capsulatum, blastomices, criptococcus y coccidioides. Se identificaron las Micobacterias por las características de las colonias, color en la oscuridad y en la luz, crecimiento a 37° y a temperatura de salón, formación de cuerdas en medios líquidos, pruebas de niacina, catalasa y rojo neutral, morfología y en algunos casos inoculación en animales experimentales. Se encontraron 20 casos positivos para Micobacterias, de los cuales 13 eran no clasificadas y 7 *Micobaeterium tuberculosis*. Las Micobacterias no clasificadas eran de los grupos I, II y III. Las características clínicas de las adenitis tuberculosas y las causadas por Micobacterias no clasificadas eran parecidas en cuanto a la duración de linfadenopatía, enfermedad anterior, fiebre y síntomas generales. Se encontraron diferencias que podrían ayudar a sospechar el diagnóstico de una u otra etiología. No había historial de contacto con tuberculosis en los casos de Micobacterias no clasificadas, mientras que la mitad de los casos de tuberculosis tenía historial de contacto. Otras características de las adenitis por Micobacterias no clasificadas eran: ausencia de casos menores de 1 año; el 60% eran niños de 20 a 24 meses de edad; casi siempre eran adenopatías unilaterales localizadas en el ángulo de la mandíbula y móviles; pruebas cutáneas demostraban erupciones débiles a la tuberculina y reacciones mayores a los antígenos preparados con Micobacterias no clasificadas. Radiografía de tórax casi siempre demostró lesiones en los niños con adenitis por *Micobacterium tuberculosis* mientras que se encontró lesión pulmonar en solamente un niño con adenitis por Micobacterias no clasificadas. Pruebas serológicas demostraron anticuerpos contra los organismos en todos los casos por Micobacterias no clasificadas aunque los casos de *Micobacterium tuberculosis* dieron reacciones cruzadas con los de Micobacterias no clasificadas. Estudios histopatológicos demostraron granulomas en la mayoría de los casos, pero no distinguieron un tipo de lesión de otro. El tratamiento incluyó en la mayoría de los casos, incisión de la glándula simultáneamente con la

biopsia e isoniacida y PAS aunque no se hicieron estudios de sensibilidad. Se informaron resultados favorables en todos los casos, y no hubo casos de seños persistentes.

J. E. SIFONTES, M. D.

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**RENAL ARTERIOGRAPHY, SEPARATE RENAL FUNCTION STUDIES AND RENAL BIOPSY IN HUMAN HYPERTENSION (Selection of Patients for Surgical Treatment)** - Arteriografía Renal, Estudios de Función Renal Separada en Hipertensión Humana (Selección de Pacientes Para Tratamiento Quirúrgico). Victor Vertes, M.D., James A. Gravel, M.D. and Harry Galblatt, M.D. (From the Mount Sinai Hospital of Cleveland), New England Journal of Medicine 270:656 - March 26, 64.

Un grupo de 52 pacientes fué sometido a arteriografía renal, estudios de función renal separada y biopsia renal bilateral. En 20 casos (38%) la arteriografía renal reveló la presencia de arterias renales anormales. En 16 casos (31%) estudios de funciones renales separadas fueron sugestivas de isquemia unilateral. En la totalidad de los 52 pacientes, se pudo comprobar por medio de la biopsia renal, enfermedad vascular intrarenal. A ninguno de estos pacientes se le hizo cirugía debido a que el autor consideró que solamente aquellos pacientes en quienes no había alteración vascular intrarenal podrían beneficiarse con la reparación de una arteria renal principal. En un paciente no incluido en esta lista, la arteriografía reveló cambios típicos de hiperplasia fibromuscular bilateral de las arterias renales, los estudios de función renal separada fueron consistentes en la demostración de isquemia renal, mientras que la biopsia de un riñón no reveló ninguna alteración significativa atribuible a enfermedad vascular intrarenal. Este paciente fué sometido a cirugía reparadora de su arteria renal y experimentó un retorno a lo normal de su presión arterial.

Los autores concluyen que la evidencia de enfermedad de la arteria renal obtenida por medio de la arteriografía renal y los estudios de función renal separada no son suficientes para poder arribar a la conclusión de que un paciente se beneficiaría con cirugía correctiva, es preciso demostrar además, por medio de la biopsia renal, que no hay enfermedad vascular intrarenal.

FERMIN MATEO TORRES, M. D.

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**SHOCK CAUSED BY GRAM-NEGATIVE MICROORGANISMS: ANALYSIS OF 169 CASES (Shock Causado por Organismos Gran Negativos).** Max Harry Weil, M.D., F.A.C.P., Herbert Schubin, M.D., F.A.C.P. and Marjorie Biddle, Ph. D., From the Department of Medicine, University of Southern California, School of Medicine and The Los Angeles County Hospital, Los Angeles, California. Annals of Internal Medicine, March 1964.

Durante el periodo de 1956-60, 692 pacientes tuvieron una bacteremias causada por organismos gram negativos en el Los Angeles County Hospital. En 169 (24%) pacientes el cuadro clínico fue complicado por shock, el cual fue más frecuente en ancianos con infección urinaria que estaban cateterizados o que habían sido sometidos a manipulación pélvica o perineal. Pacientes con diabetes mellitus o con enfermedad hepato biliar tuvieron un índice de shock más alto.

Excepto por las mujeres embarazadas, el shock fue raro en pacientes de menos de 35 años. Bacteremia fue más frecuente en mujeres mientras que bacteremia y shock fue más frecuente en hombres.

Pacientes con cateteres urinarios o heridas infectadas fueron los responsables de una tercera parte de shock en pacientes no hospitalizados. En pacientes hospitalizados algún proceso manipulativo antecedió el desarrollo de shock por no menos de 16 horas. En los pacientes que sobrevivieron, el shock duró un promedio de 2.3 días mientras que en los que murieron, el shock duró mucho más. Leucopenia y piel caliente fueron características clínicas tempranas mientras que leucocitosis y piel fría, fueron tardías.

*Escherichia coli* fue el organismo más frecuente. *Proteus* fue el organismo con la mortalidad más alta. Supervivencia fue más alta en aquellos casos en que las pruebas de sensibilidad antibióticos fueron usados para seleccionar el antibiótico.

Bacteremia tuvo una mortalidad de 20%, mientras que bacteremia y shock tuvieron una mortalidad de 82%. Pacientes con diabetes mellitus tuvieron la mortalidad más alta.

Los agentes vasopresores no tuvieron ningún efecto en mejorar la supervivencia mientras que los corticoesteroides en cantidades farmacológicas si mejoraron la supervivencia marcadamente.

ISMAEL RODRIGUEZ SANTIAGO, M. D.

## JUDICIAL COUNCIL OPINIONS AND REPORTS 1964

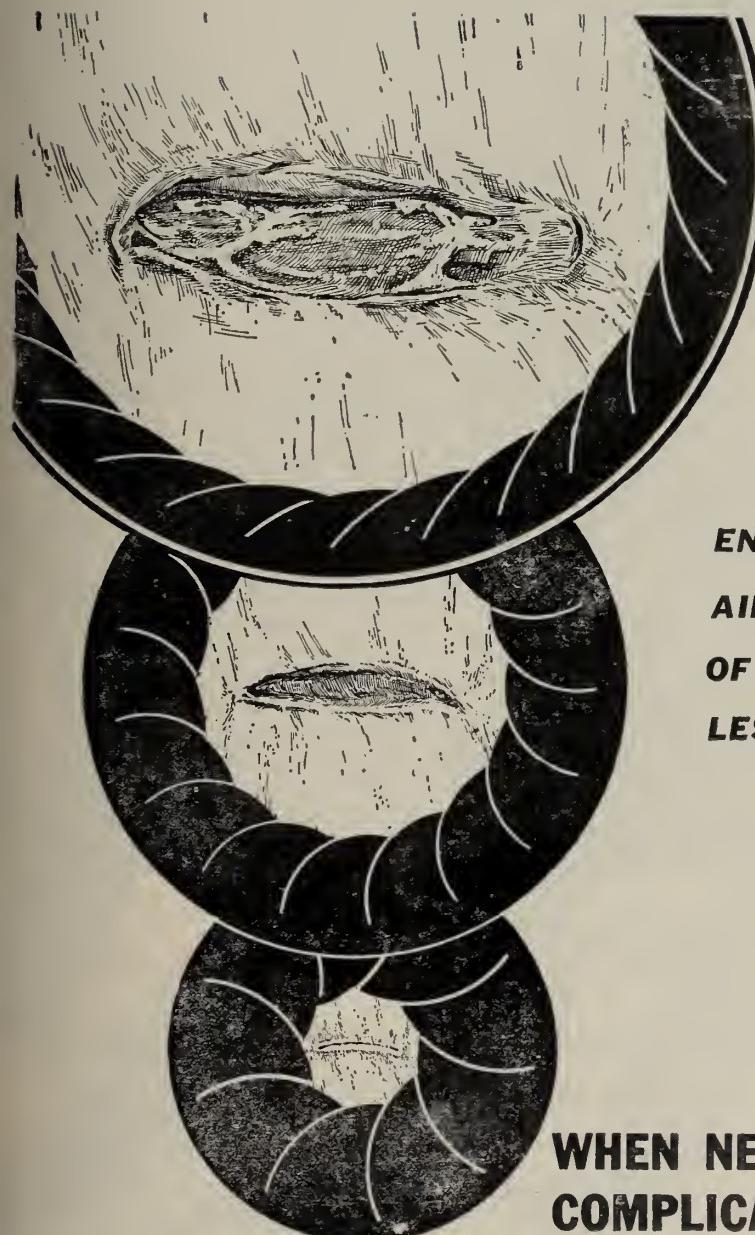
### Purveyal of Medical Service

A physician should not dispose of his professional attainments or services to any hospital, lay body, organization, group or individual by whatever name called, or however organized, under terms or conditions which permit exploitation of the services of the physician for the financial profit of the agency concerned. Such a procedure is beneath the dignity of professional practice and is harmful alike to the profession of medicine and the welfare of the people. (**Principles of Medical Ethics, 1955 edition, Chapter VII, Section 5.**)

### Purveyal of Medical Service to Direct Profit of Lay Group

The privilege of healing the sick as a profession is a right granted only to those properly qualified and licensed by the state. It is a privilege belonging only to the medical profession. It is a sacrifice of professional dignity that this exclusive right of medicine is so often sold for individual gain or its possessor deprived of it against his will. In increasing numbers, physicians are disposing of their professional attainments to lay organizations under terms which permit a direct profit from the fees or salaries paid for their services to accrue to the lay bodies employing them. Such a procedure is absolutely destructive of that personal responsibility and relationship which is essential to the best interests of the patient.

Outstanding examples of this type of unearned gain are not difficult to find. There are insurance companies administering workmen's compensation benefits wherein the salaries or fees paid to the physician by the insurance company are so much below the legal fees on which the premium paid by the industry is based as to furnish a large direct profit to the insurance company. Certain hospitals are forbidding their staffs of physicians to charge fees for their professional services to "house cases" but are themselves collecting such fees and absorbing them in hospital income. Some universities, by employing full time hospital staffs and opening their doors to the general public, charging such fees for the professional care of the patients as to net the university no small profit, are in direct and unethical competition with the profession at large and their own graduates. They are making a direct profit by a practice of questionable legality, from the professional care. (**House of Delegates, 1932**)

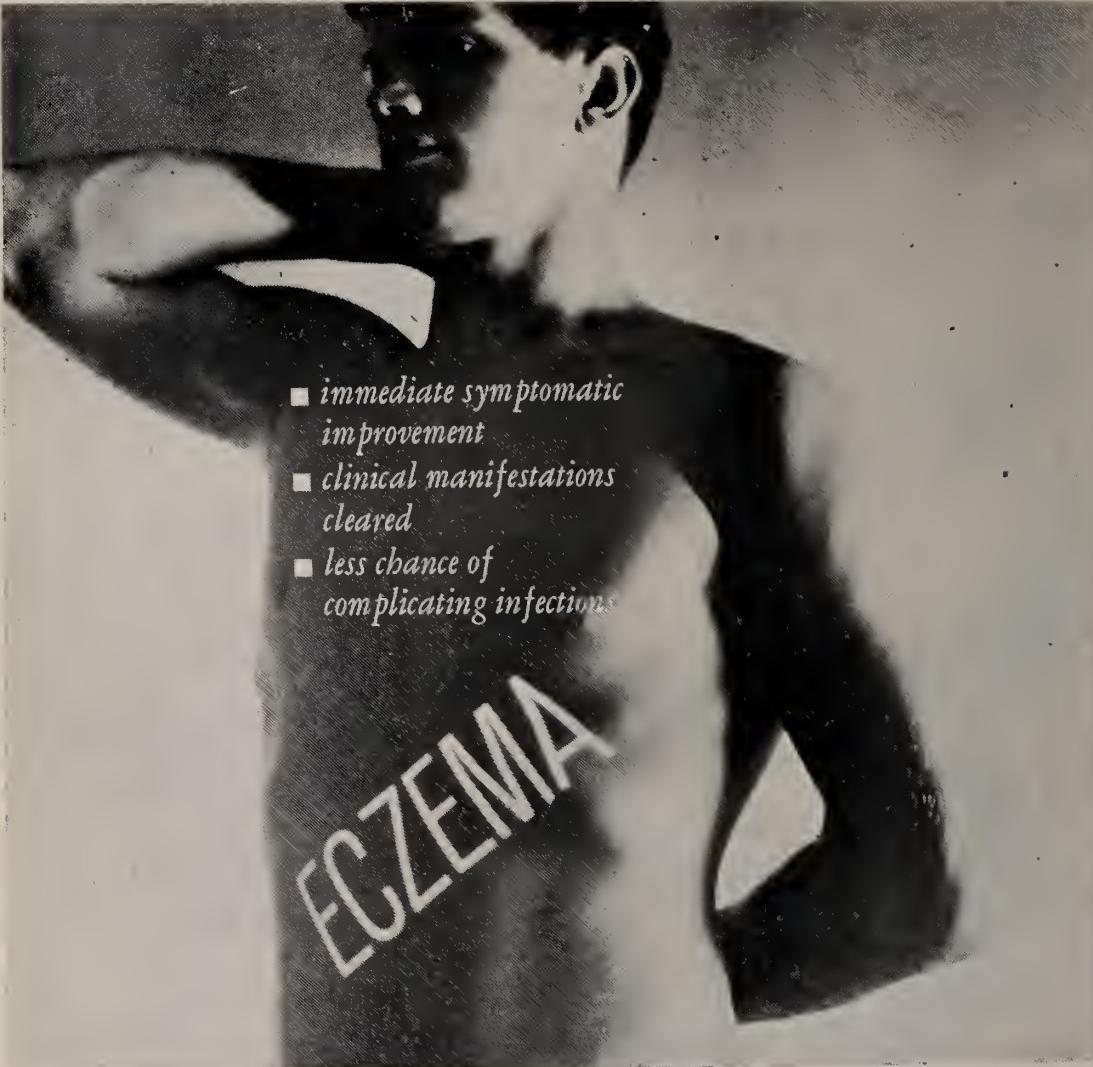


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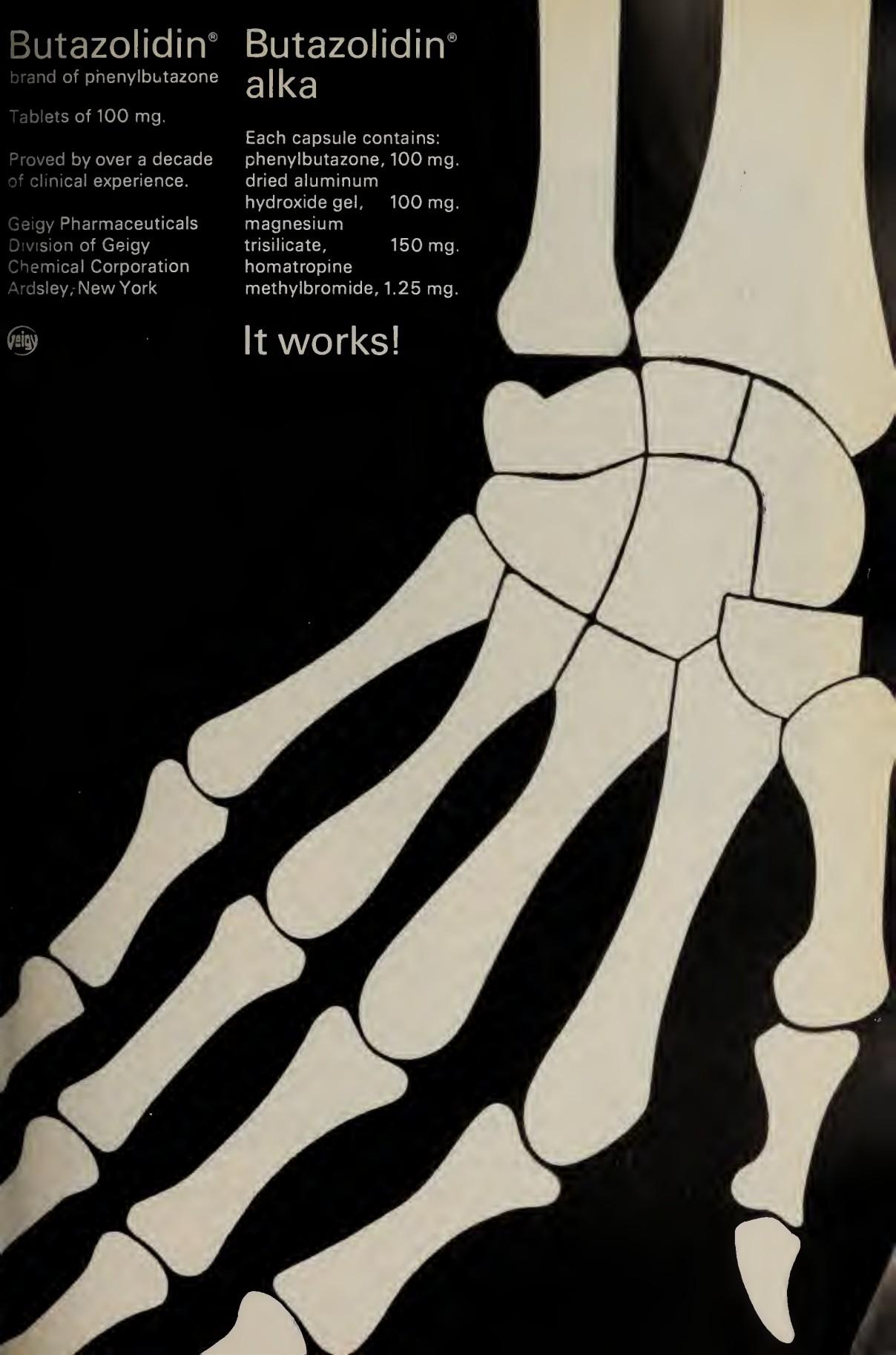
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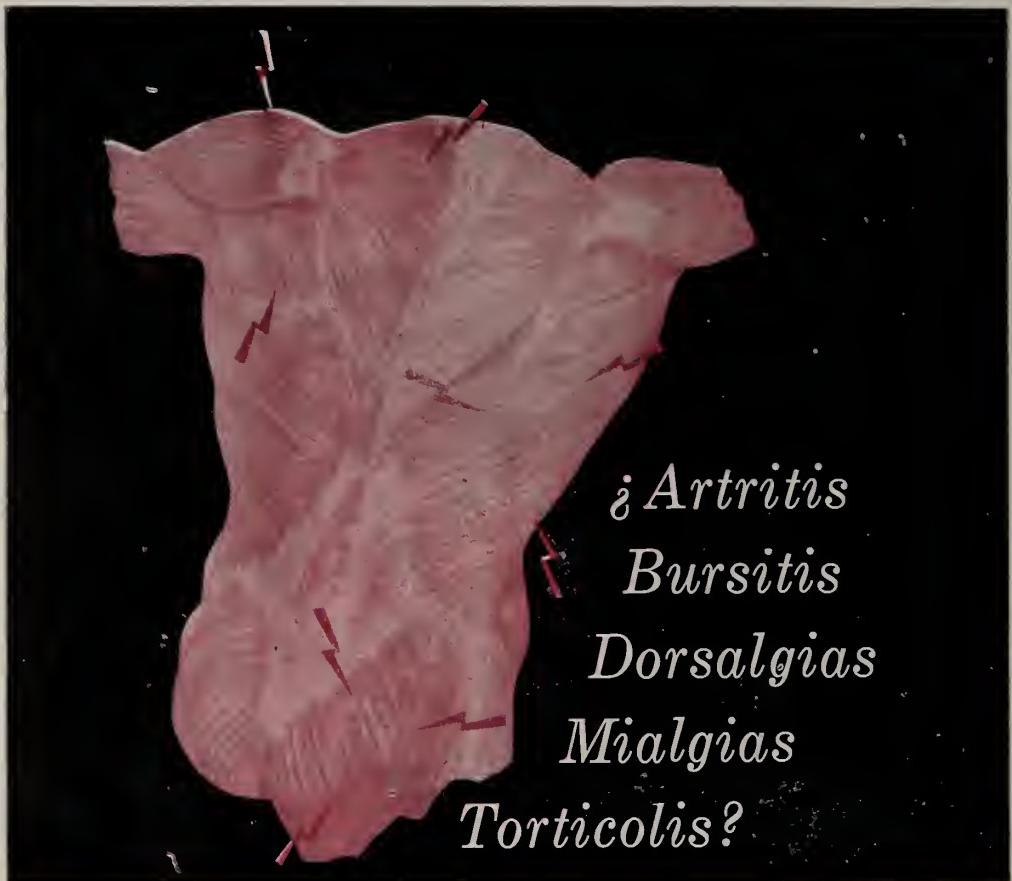
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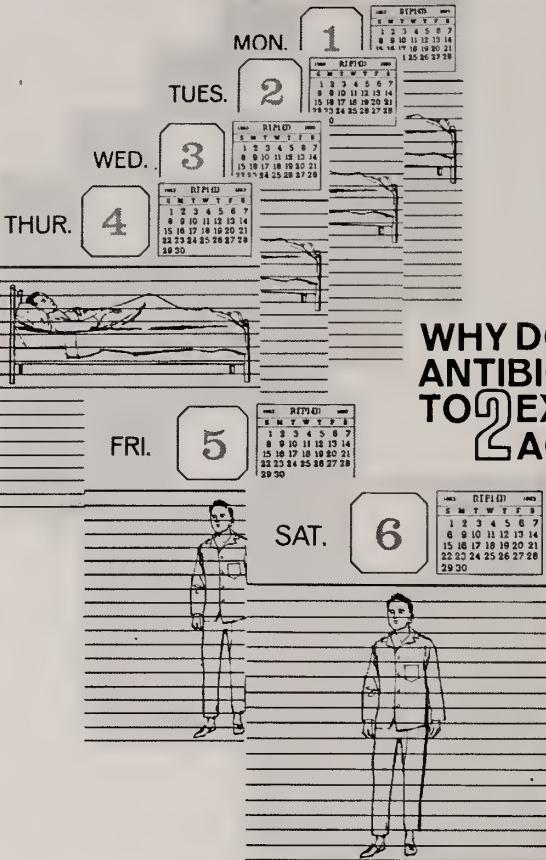
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ENTERED AS SECOND CLASS MATTER, JANUARY 21, 1931 AT THE POST OFFICE AT SAN JUAN,  
PUERTO RICO UNDER THE ACT OF AUGUST 24, 1912.

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# BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO

Fundado en el 1903 y publicado mensualmente en San Juan, Puerto Rico

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El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudieran ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor se solicita de los autores que sigan las siguientes instrucciones:

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c) Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: (1) introducción, (2) material y métodos, (3) resultados, (4) discusión, (5) resumen (en español e inglés), (6) referencias.

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f) Si un artículo ha sido leído en alguna reunión o conferencia debe así hacerse constar.

g) Deben usarse los nombres genéricos de los medicamentos. Pueden usarse también los nombres comerciales, entre paréntesis, si así se desea.

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4. Wintrobe, M. M. Clinical Hematology, 3rd Ed. Lea and Febiger, Philadelphia, 1952, p. 67. (libro)

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a) The entire manuscript, including figure legends and references, should be typewritten double-spaced in duplicate with ample margins.

b) A separate title page should include the following: title (not to exceed 80 characters and spaces), author(s) name(s) and academic degrees, institution, and authors' mailing address.

c) Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: (1) introduction, (2) material and methods, (3) results, (4) discussion, (5) summary in English and Spanish, (6) references.

d) Case reports will include (1) introduction, (2) description of the case, (3) discussion, (4) summary in English and Spanish and (5) references.

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g) Generic names of drugs should be used. Trade names may also be given in parenthesis if desired.

h) Metric units of measurements should be used preferentially. Abbreviations should be used sparingly.

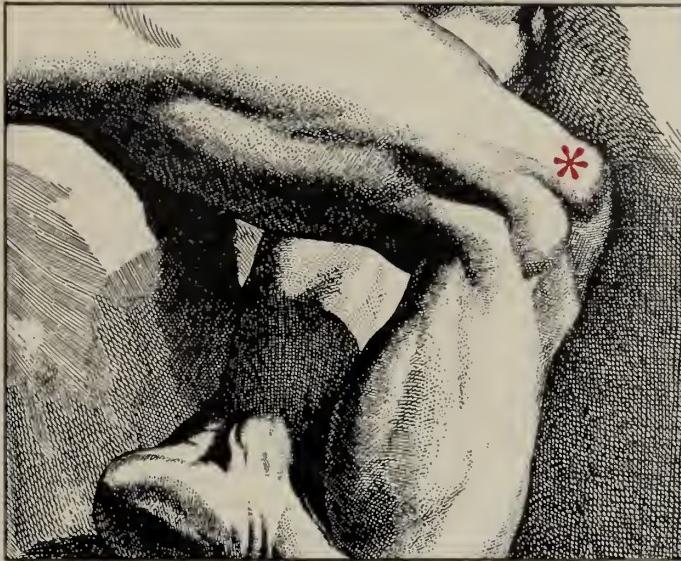
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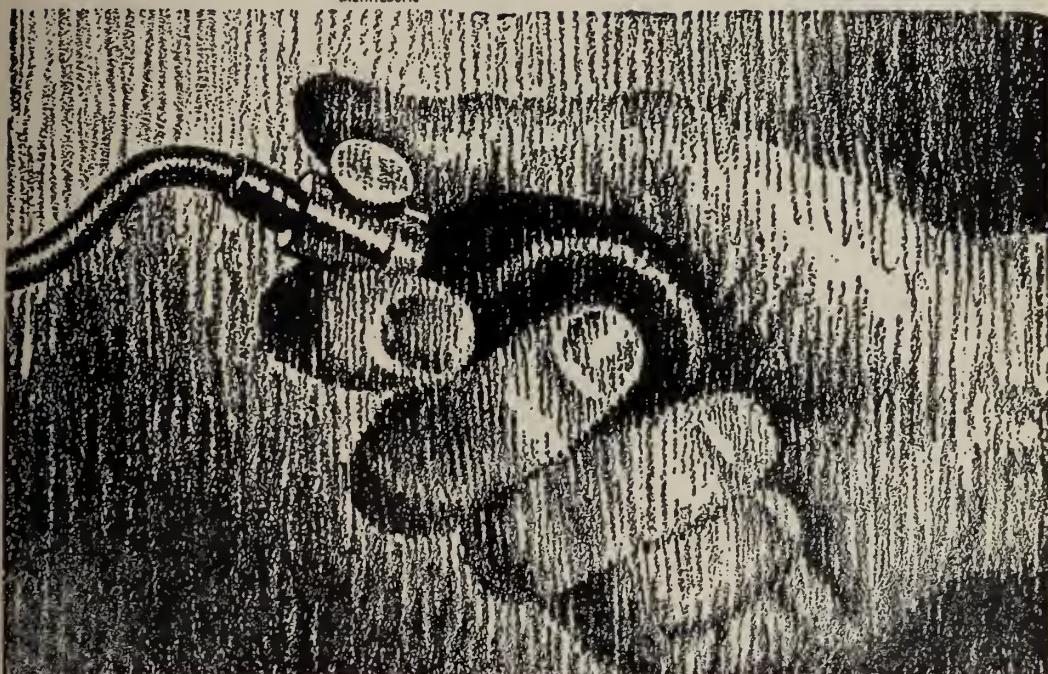
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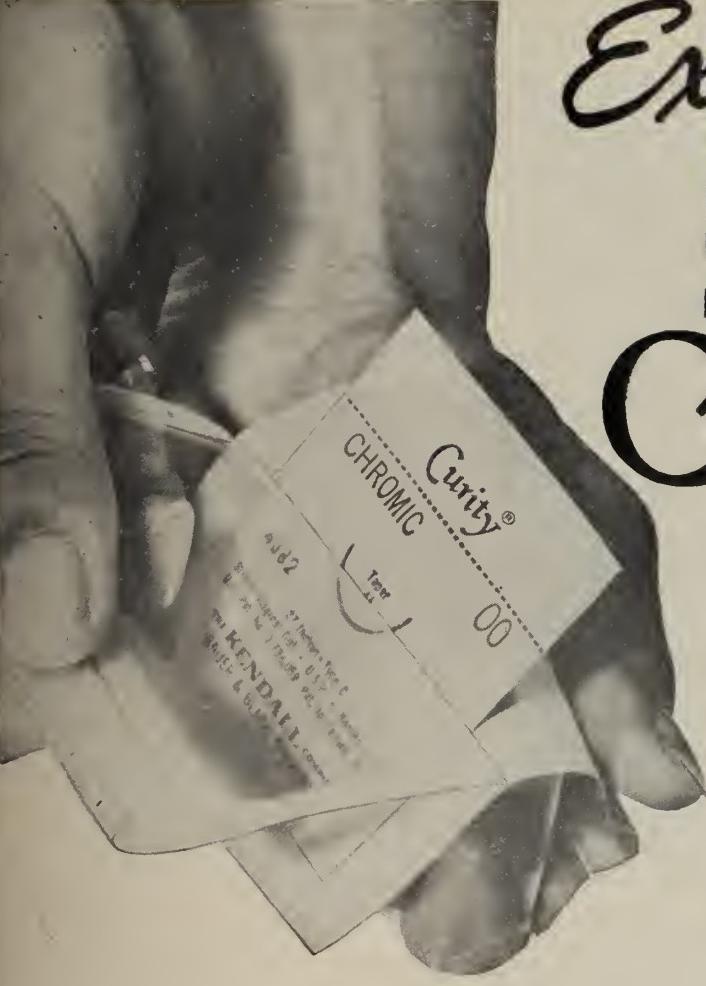
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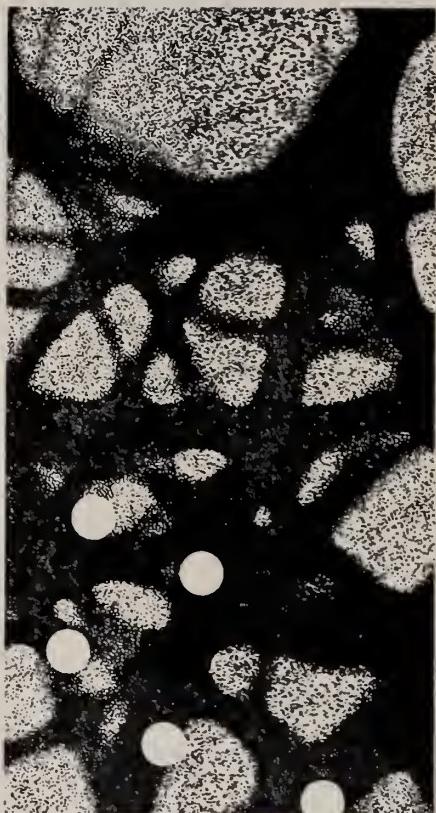


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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



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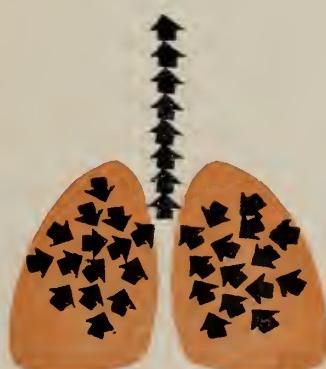
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**Precautions:** Anuria.

\*From clinical data on file at Lederle Laboratories. Posed by model.

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# BOLETIN

DE LA ASOCIACION MEDICA DE PUERTO RICO

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VOL. 56

JULIO, 1964

No. 7

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## INCIDENCE OF HEART DISEASE IN PUERTO RICO (A CLINICAL AND PATHOLOGIC STATISTICAL STUDY)\*

FEDERICO DIEZ RIVAS, M.D.

MANUEL A. DE JESUS, M.D.

During the last fifty years the annual number of deaths from heart disease in Puerto Rico has shown a slight increase yet the precipitous drop in the general mortality has placed the diseases of the heart as the leading cause of death in this island. As shown in Figure I this same situation has occurred in the United States although it has been more alarming because even though the general mortality rate was less the mortality rate for heart disease has been twice as high as in Puerto Rico.

Because of the importance of heart disease as a cause of death in Puerto Rico, several publications on this subject have appeared in the literature during the past 18 years. In 1945, Suárez,<sup>1</sup> reported on the etiologic classification of heart disease in Puerto Rico. In 1946, Francisco<sup>2</sup> reported on the incidence of rheumatic heart disease in the island. Last year, García Palmieri et al.<sup>3</sup> wrote on the subject of rheumatic fever in the tropics. Rodríguez et al<sup>4</sup> reported on the incidence of heart disease at the Cardiovascular Clinic of the Ponce District Hospital and analyzed 2000 autopsies performed at the same hospital.

The purposes of this study are as follows:

1. To determine the incidence of the different types of heart disease among 2433 cases with organic heart disease seen at the Cardiovascular Clinic of the San Juan City Hospital during the period 1952 to 1962.

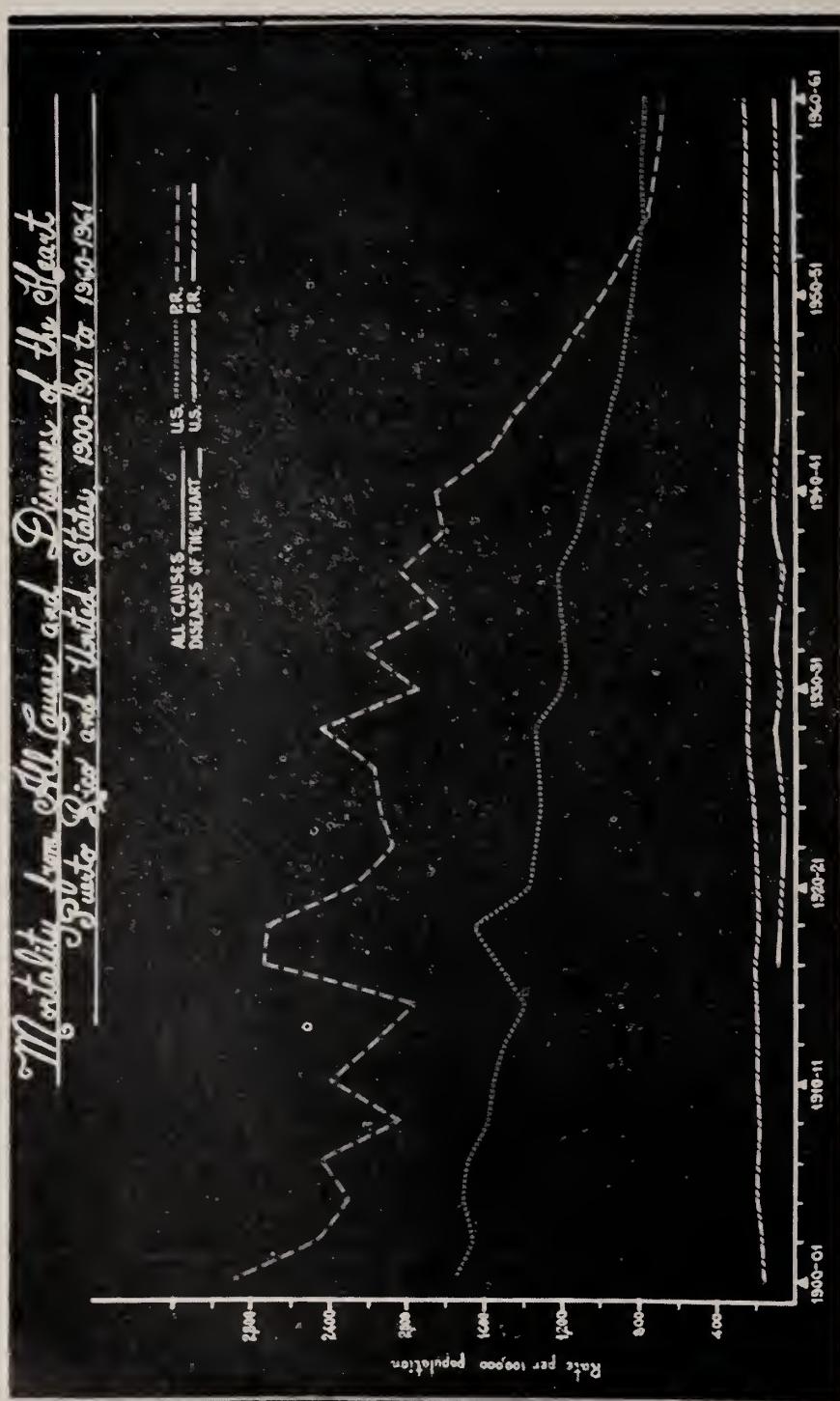
2. To determine the incidence of the different types of heart disease among 2131 autopsies performed at the San Juan City Hospital during the years 1955 to 1963 and to compare these findings with other similar studies reported in the literature.

3. To compare our clinical and autopsy findings.

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\* From the Cardiovascular Clinic and the Pathology Department of the San Juan City Hospital.

Presented at the Annual Meeting of the Puerto Rico Heart Association, May, 1963.



4. To compare our clinical findings with those obtained at the other Cardiac Clinics of the Heart Control Program throughout the island.

5. To compare our clinical and pathologic findings with the reports on mortality obtained from the Bureau of Demographic Registry and Vital Statistics of the Puerto Rico Department of Health.

The data to be presented includes all ages and both sexes.

The nomenclature and criteria for the diagnosis of the different types of heart disease used in this study were those recommended by the Criteria Committee of the New York Heart Association.<sup>5</sup>

## RESULTS

### A. Clinic Material Studied.

I. Analysis of the cases seen at the Cardiovascular Clinic of the San Juan City Hospital. (Table I)\*

During the period 1952 to 1962 a total of 4560 patients have been studied at this clinic. Of this group, 2433 patients (53.3%) were found to have organic heart disease and 847 cases (18.5%) were found to be free of heart disease. Of the 2433 cases with organic heart disease, 1017 cases (41.8%) were found to have arteriosclerotic heart disease, 529 cases (21.7%) had hypertensive heart disease, 395 cases (16.2%) had rheumatic heart disease, 390 cases (16.0%) had congenital heart disease, 78 cases (3.2%) were found to have syphilitic heart disease and 24 cases (.98%) had other types of heart disease.

An analysis of the annual number of cases of each one of these categories of heart disease reveals little significant variation (average and median values are similar); nevertheless, the arteriosclerotic, rheumatic and syphilitic groups have decreased while the congenital group has increased.

If we compare our findings with those of Suárez<sup>1</sup> (Table II) compiled during the years 1937-1944 and published in 1945, we see that the clinical incidence of arteriosclerotic, hypertensive and

\* The following abbreviations have been used in the tables presented.

OHD — Organic heart disease.

ASHD — Arteriosclerotic heart disease.

HHD — Hypertensive heart disease.

RHD — Rheumatic heart disease.

SHD — Syphilitic heart disease.

CHD — Congenital heart disease.

CV — Cardiovascular.

Rh.F. — Rheumatic fever.

TABLE I  
ADMISSIONS TO CV — CLINIC AT S.J.C.H. (FY-1952-1962)

Fiscal Years	Total No. of Persons Seen	Cases with Org. H.D.	TYPES OF HEART DISEASE				Poss H.D.	Pot H.D.	Neg.	Pending
			HHD	ASHD	RHD	SHD				
1952	377	270	44	159	46	13	7	1	10	3
1953	473	328	69	151	53	16	37	2	2	31
1954	471	246	49	102	46	10	36	3	45	115
1955	630	279	81	109	44	9	34	2	21	60
1956	481	217	61	92	30	7	24	3	6	26
1957	405	207	60	88	27	4	25	3	16	18
1958	349	161	23	51	42	6	38	1	15	25
1959	311	167	32	66	23	3	41	2	8	25
1960	278	148	21	44	26	4	49	4	2	22
1961	368	193	37	82	27	4	42	1	9	40
1962	417	217	52	73	31	2	57	2	8	48
Totals	4560	2433	529	1017	395	78	390	24	97	343
Median	405	217	49	88	31	6	37	2	8.5	26
Average	414	221	48	92	36	7	35	2	9.7	31
%	53.3	21.7	41.8	16.2	3.2	16.0	.98	2.1	7.5	18.5
										18.4

No. of cases of Essential Hypertension without OHD.—92  
No. of cases of Rheumatic Fever without OHD.—45

TABLE II  
TYPES OF HEART DISEASE

Etiology	Suárez - 1945 (1937-1944)	San Juan City Hospital
	1081 cases	1952-1962 - 2433 cases All ages - Both sexes
Arteriosclerosis	40%	41.8%
Hypertension	22.8%	21.7%
Rheumatic	17.4%	16.2%
Congenital	1%	16.0%
Syphilitic	6.1%	3.2%
Miscellaneous	10.2%	.98%

rheumatic heart disease has remained the same throughout the past 25 years, while syphilitic heart disease has decreased but the group with congenital heart disease has increased.

These two variations could be explained on the basis of a better control of early syphilis and a decrease in infant mortality during this same period. In 1937 there were 9,404 infant deaths. Only 3,108 occurred in 1961.<sup>8</sup>

#### II. Analysis of the cases seen at the Cardiac Clinic of the Ponce District Hospital. (Table III):

During the period 1960 to 1962 a total of 1688 cases were studied. Eight hundred and eleven (48%) were found to have organic heart disease. Among the organic group, 379 cases (46.7%) had arteriosclerotic heart disease, 217 cases (26.7%) had hypertensive heart disease, 95 cases (11.3%) had congenital heart disease, 11 cases (1.3%) had syphilitic heart disease and 17 cases (2%) had other types of heart disease.

#### III. Analysis of the cases seen at the Cardiac Clinic of the Mayagüez Public Health Unit. (Table IV):

During the period from 1959 to 1962 a total of 943 patients were studied in that clinic. From this group, 497 cases (52.7%) were found to have organic heart disease. In this latter group 181 cases (36.4%) had arteriosclerotic heart disease, 158 cases (31.7%) had congenital heart disease, 63 cases (12.6%) had hypertensive heart disease, 52 cases (10.4%) had rheumatic heart disease, 23 cases (4.6%) had syphilitic heart disease and 20 cases (4%) had other types of heart diseases.

#### IV. Analysis of the cases seen at the Cardiac Clinic of the Arecibo District Hospital. (Table V):

During the period from 1960 to 1962, a total of 694 persons were examined at this clinic. Of this group, 303 cases (43.6%) were found to suffer from organic heart disease. In this organic group, 109 cases (35.9%) had arteriosclerotic heart disease, 69 cases (22.7%) had congenital heart disease, 60 cases (19.8%) had

TABLE III  
ADMISSIONS TO CARDIAC CLINIC AT PONCE DISTRICT HOSPITAL (FY-1960-62)

Fiscal Years	Total No. of Persons Seen	Cases with Org. H. D.	TYPES OF HEART DISEASE						Poss H. D.	Pot H. D.	Neg.	Pending
			HHD	ASHD	RHD	SHD	CHD	Other				
1960	480	252	76	114	31	6	18	7	6	56	121	45
1961	641	264	59	129	37	2	31	6	8	77	144	148
1962	567	295	82	136	27	3	43	4	5	51	87	129
Totals	1688	811	217	379	95	11	92	17	19	184	352	322
%		48.0	26.7	46.7	11.7	1.3	11.3	2.0	1.1	10.9	20.8	19.0

No. of cases of Essential Hypertension without O.H.D.—3  
No. of cases of Rheumatic Fever without O.H.D.—54

TABLE IV  
ADMISSIONS TO CARDIAC CLINIC AT MAYAGUEZ PUBLIC HEALTH UNIT (FY-1959-62)

Fiscal Years	Total No. of Persons Seen	Cases with Org. H. D.	TYPES OF HEART DISEASE						Poss H. D.	Pot H. D.	Neg.	Pending
			HHD	ASHD	RHD	SHD	CHD	Other				
1959	190	110	19	38	12	10	27	4	3	13	44	20
1960	284	174	21	66	24	6	45	12	9	5	81	15
1961	179	98	11	35	10	4	35	3		8	52	21
1962	290	115	12	42	6	3	51	1	2	8	125	40
Totals	943	497	63	181	52	23	158	20	14	34	362	96
%		52.7	12.6	36.4	10.4	4.6	31.7	4.0	1.4	3.6	32.0	10.1

No. of cases of Essential Hypertension without O.H.D.—0  
No. of cases of Rheumatic Fever without O.H.D.—4

rheumatic heart disease, 57 cases (18.8%) had hypertensive heart disease, 4 cases (1.3%) had syphilitic heart disease and 4 cases (1.3%) had other varieties of organic heart disease.

If we compare the results obtained at the four Cardiac Clinics (Table VI) throughout the island the following important points should be mentioned:

1. The most frequent cause of heart disease in all the clinics was arteriosclerotic heart disease. The incidence of this category was approximately the same at our clinic as at the Cardiac Clinic of the Ponce District Hospital. The incidence at the Mayaguez and Arecibo Clinics was similar.

2. The second most important cause of heart disease both at the Mayaguez and Arecibo Cardiac Clinics was congenital heart disease, being twice as high as at the Ponce Clinic or our clinic. This higher incidence could be due to lack of specialized diagnostic facilities (cardiac catheterization, angiography, etc.) for a more complete evaluation of these cases. Both at our clinic and at the Ponce clinic the second most important category was hypertensive heart disease.

3. The third most important category of heart disease at our Clinic as well as at the Ponce and the Arecibo clinics was rheumatic heart disease while at the Mayaguez Clinic, the third cause of heart disease was hypertensive heart disease.

4. The fourth cause of heart disease both at our clinic and at the clinic in Ponce was congenital heart disease while at the Mayaguez Clinic the fourth cause was rheumatic heart disease. This clinic had the lowest incidence of rheumatic heart disease among all the four clinics. The fourth type of heart disease at the Arecibo clinic was hypertensive heart disease.

5. The fifth cause of heart disease in all the four clinics was syphilitic heart disease. The highest incidence of this type of heart disease was found at the clinic in Mayaguez (4.6%). The lowest incidence was found at the Ponce and Arecibo clinics where it accounted for (1.3%) of the cases with heart disease. At our clinic the incidence was (3.2%).

## B. Pathologic Material Studied.

### I. Analysis of autopsy findings at the San Juan City Hospital

During the period of September, 1955 to March, 1963, a total of 2131 autopsies were performed by the Pathology Department of this hospital under the direction of Dr. Manuel de Jesús. Of this group comprising all ages and both sexes, 431 cases (20.2%) were found to have organic heart disease. In the group with heart disease 216 cases (50.1%) were found to have arteriosclerotic

TABLE V  
ADMISSIONS TO CARDIAC CLINIC AT ARECICO DISTRICT HOSPITAL (EX. 1960-62)

Fiscal Years	Total No. of Persons Seen	Cases with Org. H. D.	TYPES OF HEART DISEASE						Poss H. D.	Pot H. D.	Neg.	Pending
			HHD	ASHD	RHD	SHD	CHD	Other				
1960	184	98	22	39	21	2	14		15	9	58	4
1961	225	92	13	31	14	1	31	2	19	25	81	8
1962	285	113	22	39	25	1	24	2	27	25	62	58
Total	694	303	57	109	60	4	69	4	61	59	201	70
%		43.6	18.8	35.9	19.8	1.3	22.7	1.3	8.7	8.5	28.9	10.0

No. of cases of Essential Hypertension without O.H.D.—3  
No. of cases of Rheumatic Fever without O.H.D.—4

TABLE VI  
TOTAL ADMISSIONS TO ALL CLINICS (H.C.D.)

Clinics & Years	Total No. Persons Seen	No. Cases with H.D.	TYPES OF HEART DISEASE				Poss. H. D.	Pot. H. D.	Neg. H. D.	Pend- ing	HYP & Other H.D.	Ess.	
			HHD	ASHD	RHD	SHD	CHD	Other					
S.J.C.H. 1952-62	4560	2433	529	1017	395	78	390	24	97	343	847	840	92
FY	100%	53.3	21.7	41.8	16.2	3.2	16.0	.92	2.1	7.5	18.5	18.4	2.0
Ponce Dist. Hospital	1688	811	217	379	95	11	92	17	19	184	352	322	3
FY-1960-62	100%	48.0	26.7	46.7	11.7	1.3	11.3	2.0	1.1	10.9	20.8	19.0	1.8
M.La.yaguez P.I.D.	943	497	63	181	52	23	158	20	14	34	302	96	4
FY-1959-62	100%	52.7	12.6	36.4	10.4	4.6	31.7	4.0	1.4	3.6	32.0	10.1	0
Arecibo Dist. Hospital	694	303	57	109	60	4	69	4	61	59	201	70	3
FY-1960-62	100%	43.6	18.8	35.9	19.8	1.3	22.7	1.3	8.7	8.5	28.9	10.0	.46

TABLE VII  
AUTOPSY MATERIAL ALL AGES AND BOTH SEXES

Type of Org. Heart	San Juan City			Ponce Dist. Hos-		School of Tropical	
	Hospital 1955-63		% of	pital 1956-62		Medicina 1944—	
	2131 autopsies		Total	2000 autopsies		1259 autopsies	
Disease	No.	% OHD	% of Total	No.	%	No.	%
Arteriosclerotic	216*	50.1	10.1	133**	32	22	17
Arteriosclerosis						12	9.3
Arteriosclerotic Hypertensive				53	12.8		
Congenital	81	18.8	3.85	83	20	10	7.8
Hypertensive	45	10.45	2.11	41	9.9		
Rheumatic	34	7.89	1.55	32	7.7	26	20
Syphilitic	7	1.62	.33			38	30
Cor Pulmonale	13	3.02	.61	31	7.5		
Miscellaneous	35	8.1	1.6	42	10.1		

\* 45 cases of Myocardial infarction included.

\*\* 56 cases of Myocardial infarction included.

heart disease. Among this latter group there were 45 cases with myocardial infarctions. There were 81 cases (18.8%) with congenital heart disease, 45 cases (10.45%) with hypertensive heart disease, 34 cases (7.89%) with rheumatic heart disease, 7 cases (1.62%) with syphilitic heart disease, and 13 cases (3.02%) with cor pulmonale. There were 35 cases (8.1%) with miscellaneous types of heart disease among which 11 cases (2.55%) had fibro-elastosis fetalis, 6 cases (1.39%) had acute bacterial endocarditis, 3 cases (.69%) had subacute bacterial endocarditis, 4 cases (.92%) had metastatic tumors, 3 cases (.69%) had bacterial myocarditis, 2 cases (.46%) had idiopathic myocarditis, 3 cases (.69%) had constrictive pericarditis, 1 case of rhabdomyoma, 1 case of amyloidosis and, 1 case of idiopathic hypertrophy of the heart.

## II. Autopsy findings at the Ponce District Hospital.

These findings were reported recently by Rodríguez et al<sup>4</sup> and are summarized in table VII. Of the 2000 autopsies performed during the period 1956 to 1962, 415 cases (20.7%) were found to have organic heart disease. Among this group with heart disease there were 133 cases (32%) with arteriosclerotic heart disease and 53 cases (12.8%) with arteriosclerotic hypertensive heart disease, both forming a group of 186 cases (44.8%) of arteriosclerotic heart disease. Among this group there were 56 cases of myocardial infarctions. There were 83 cases (20%) of congenital heart disease, 41 cases (9.9%) of hypertensive heart disease, 32

cases (7.7%) of rheumatic heart disease, 31 cases (7.5%) of cor pulmonale and 42 cases (10.1%) of other types of heart disease.

Comparing these findings with those from our series reveals that the incidence of arteriosclerotic heart disease at our hospital (50.1%) was about the same as at the Ponce District Hospital (44.8%). At our hospital the incidence of cor pulmonale was (3.02%) while in the Ponce series it was (7.5%). The other categories of heart disease were very similar in both series.

III. Autopsy findings at the School of Tropical Medicine (See Table VII). Koppisch's<sup>6</sup> post mortem studies on 1259 autopsies performed at this institution were reported by Suárez in 1945. Of this series, 128 cases (10%) were found to have organic heart disease. Among this group, 38 cases (30%) had syphilitic heart disease, 23 cases (20%) had rheumatic heart disease, 22 cases (17%) had arteriosclerotic heart disease, 10 cases (7.8%) had congenital heart disease, 10 cases (7.8%) had subacute bacterial endocarditis, 7 cases (5.5%) had acute bacterial endocarditis and 15 cases (11.4%) had miscellaneous diseases affecting the cardiovascular system.

Comparing this series with ours and with the series from the Ponce District Hospital reveal the following important observations:

1. A lower incidence of organic heart disease in Koppisch's series (10%) than in our series and in the Ponce District Hospital series (20%).
2. There has been marked decrease in the incidence of syphilitic heart disease, from (30%) in Koppisch's series to (1.62%) in our hospital series.
3. There has been a marked increase in incidence in arteriosclerotic heart disease from 17% in Koppisch's series to 50.1% in our series and 44.8% in the series from the Ponce District Hospital. This same observation was reported in 1958 by Lichtenberg and Galindo.<sup>7</sup>
4. There has been a marked decrease in the incidence of rheumatic heart disease from 20% in Koppisch's series to 7.8% both in our hospital series and the series from the Ponce District Hospital.
5. There has been a considerable increase in the incidence of congenital heart disease from 7.8% in Koppisch's series to 18.8% in our series and 20% in the series from the Ponce District Hospital.
6. A marked decrease has occurred in the incidence of subacute bacterial endocarditis from 7.8% in Koppisch's series to .69% in our hospital series.

All these important changes have been due to a multiplicity of factors the most important being the antibiotics. The tremen-

dous increase in the incidence of arteriosclerotic heart disease is probably a reflection of the decrease in mortality from other heart diseases as well as a decrease in the general mortality of the population as a whole or could be due to a real increase of arteriosclerosis.

### C. Report of the Bureau of Demographic Registry and Vital Statistics: Puerto Rico Department of Health.<sup>8</sup>

A review of 1951 Annual Report on Vital Statistics published by the Bureau of Demographic Registry and Vital Statistics of the Puerto Rico Department of Health reveals that the annual number of cardiac deaths in the island has shown little variation during the past ten years. During this period there has been a slight decrease in the total number of deaths. During the period from 1950 to 1951, there were 212,672 deaths in the island. Of this total number of deaths, 31,492 persons (14.8%) died from heart disease. Among the cardiac deaths, 21,348 persons (67.6%) were reported as dying from arteriosclerotic heart disease, 4,457 persons (14.1%) died from hypertensive heart disease, 1,073 persons (3.4%) died from rheumatic heart disease and 4,714 persons (14.9%) died from other heart diseases. Only 315 persons (1%) presumably died from acute rheumatic fever without heart disease.

From this report the three most important categories of heart disease are arteriosclerotic heart disease, hypertensive heart disease and rheumatic heart disease. No data was available on the deaths from congenital heart disease as such but it was probably included among the group of other heart disease that accounted for 4,714 deaths (14.9%) during this 12 years period.

These three categories of heart disease were the three most important ones in our clinic series and in the autopsy series except that in this last one the congenital heart diseases ranked second in importance. It has been very gratifying for all of us working at the different cardiac clinics to find such a good correlation among the only available sources of information on the incidence of heart disease in Puerto Rico. (Table IX).

### Summary and Conclusions:

In order to obtain a better picture of the true incidence of the different types of heart disease in Puerto Rico the clinical and pathologic material from the San Juan City Hospital was compared with similar data from other hospital throughout the island. This data was correlated with the reported incidence from the Bureau of Demographic Registry and Vital Statistics of the Puerto Rico Department of Health.

TABLE VIII  
CARDIAC DEATHS BUREAU OF DEMOCRATIC REGISTRY P. R. DEPT. OF HEALTH

Year	C. V. and				HHD				RHD				Other H.D.				Rheumatic			
	Total Deaths	Rh. F	Cardiac Deaths	ASHD %	Deaths	%	HHD Deaths	%	Deaths	%	Deaths	%	Deaths	%	Deaths	%	Fever			
1950	21917	2869	2404	1554	64.6	353	14.6	103	4.2	394	16.3	28				.97				
1951	22371	3039	2566	1627	63.4	365	14.2	125	4.8	449	17.4	23				.75				
1952	26504	2883	2498	1638	65.5	409	16.3	87	3.5	364	14.5	33				1.1				
1953	17966	2897	2532	1672	66.0	392	15.4	102	4.0	366	14.4	42				1.4				
1954	16871	2761	2390	1565	65.4	341	14.2	90	3.7	394	16.4	35				1.2				
1955	16243	2712	2352	1450	61.6	401	17.0	79	3.3	422	17.9	28				1.0				
1956	16667	3071	2539	1763	69.4	340	13.3	91	3.5	445	17.5	26				.84				
1957	16022	3121	2694	1864	69.1	327	12.1	73	2.7	430	15.9	26				.83				
1958	16099	3077	2654	1834	69.1	394	14.8	68	2.5	358	13.4	17				.55				
1959	15870	3278	2486	2037	71.5	386	13.5	65	2.2	358	12.5	15				.45				
1960	15841	3314	2820	2070	73.4	360	12.7	85	3.0	305	10.8	18				.54				
1961	16361	3750	3197	2274	71.1	389	12.1	105	3.2	429	13.4	24				.64				
Total	212672		31492	21348	67.6	4457	14.1	1073	3.4	4714	14.9	315				1.0				
Median	16484		2552	1717		375			88		394		26							
Average	17723		2624	1779		371			89		393		26							

TABLE IX  
COMPARISON OF RELATIVE FREQUENCIES OF ORGANIC HEART DISEASE IN P. R.

Source	No. of Cases	TYPES OF HEART DISEASE													
		O.H.D.	ASHD	HHD	RHD	CHD	SHD	Other	No.	%	No.	%	No.	%	
Clinic Mat. (S.J.C.H.) FY-1962-62	4560	2433	53.3	1017	41.8	529	21.7	395	16.2	390	16.0	78	3.2	24	.98
Autopsy Mat. (S.J.C.H.) 1955-1963	4560	2433	53.3	216	50.12	45	10.45	31	7.89	81	18.8	7	1.62	48	11.1
Bureau of Demographic Registry (Dept. of H.) 1950-1961	212672	31492	14.8	21348	67.6	4457	14.1	1073	3.4					4714	14.9

Of 4,560 patients studied at the Cardiovascular Clinic of the San Juan City Hospital during the period 1952 to 1962; 2,433 cases (53.3%) were found to have organic heart disease. Of this group 41.8% were arteriosclerotic; 21.7% were hypertensive; 16.2 were rheumatic; 16% were congenital and 3.2% were syphilitic in origin.

Among 2,131 autopsies performed in this same hospital during the period 1955 to 1963; 431 cases (20.2%) were found to have organic heart disease. Of this group 50.12% were arteriosclerotic; 18.8% were congenital; 10.45% were hypertensive; 7.89% were rheumatic and 1.62% were syphilitic in origin.

A similar incidence has been reported among 2,000 autopsies performed at the Ponce District Hospital during the period 1956 to 1962.

Data from the Bureau of Demographic Registry and Vital Statistics of the Puerto Rico Department of Health reveal that during the period 1950 to 1961; 14.8% of the total number of deaths in Puerto Rico were due to cardiac disease this being the leading cause of death in the island. Of these cardiac deaths, 67.6% were arteriosclerotic; 14.1% were hypertensive; 3.4% were rheumatic and 14.9% were due to other cardiac ailments.

The most important type of heart disease in all the cardiac clinics throughout the island is arteriosclerotic which accounts for approximately 40 to 50% of the cases. This incidence has been confirmed by the pathologic findings both at the San Juan City Hospital and the Ponce District Hospital as well as by the Death Registry.

The second most important type of heart disease at our cardiac clinic and at the Ponce District Hospital was hypertensive heart disease, accounting for approximately 21% of the cases. At the Mayagüez and Arecibo cardiac clinics the second most important type was congenital heart disease accounting for approximately 22 to 32% of the cases studied.

The third and fourth important types of heart disease at our clinic as well as at the Ponce District Hospital were rheumatic and congenital heart disease, each category accounting for approximately 11 and 16% of the total at these two clinics respectively. At the Mayaguez and Arecibo clinics the third and fourth important types were the rheumatic and hypertensive heart disease. In the autopsy series from our hospital (and from the Ponce District Hospital) congenital heart disease (18.8%) ranked second in importance while the hypertensive group (10.45%) ranked third and rheumatic heart disease (7.89%) fourth.

The fifth important type of heart disease both in our clinic material (3.2%), as well as the pathologic material (.62%) was syphilitic heart disease. This category was also the fifth important type of heart disease among all the other cardiac clinics throughout the island both clinically and pathologically (Ponce District Hospital).

#### RESUMEN

Para obtener una mejor idea de la incidencia de los distintos tipos de enfermedades del corazón en Puerto Rico el material clínico y patológico del Hospital Municipal de San Juan ha sido comparado con información similar obtenida de otros hospitales de la isla. Esta información ha sido también comparada con las estadísticas del Negociado del Registro Demográfico y Estadísticas Vitales del Departamento de Salud de Puerto Rico.

De 4,580 pacientes estudiados en la clínica cardiovascular del Hospital Municipal de San Juan durante el período 1952 al 1962; 2,483 casos (53.3%) fueron encontrados con enfermedad orgánica del corazón. En este grupo el 41.8% fueron arterioscleróticos; 21.7% hipertensos; 16.2% reumáticos; 16% congénitos y 3.2% sifilíticos.

Entre 2,131 autopsias hechas en este mismo hospital durante el período 1955 al 1963; 431 casos (20.2%) fueron encontrados con enfermedad orgánica del corazón. En este grupo el 50.12% fueron arterioscleróticos; 18.8% congénitos; 10.45% hipertensos; 7.89% reumáticos y 1.62% sifilíticos.

Una incidencia similar ha sido informada de 2,000 autopsias hechas en el Hospital de Distrito de Ponce durante el período 1955 al 1962.

Información obtenida del Negociado de Registro Democrático y Estadísticas Vitales del Departamento de Salud de Puerto Rico revela que durante el período de 1950 al 1961; 14.8% de las muertes totales en Puerto Rico se debieron a enfermedad del corazón, siendo así la causa principal de muerte en la isla. De estas muertes cardíacas; 67.6% fueron debido a arteriosclerosis; 14.1% hipertensos; 3.4% reumáticos y 14.9% debidos a otras enfermedades del corazón.

La causa más importante de enfermedad del corazón en todas las clínicas de la isla es la arteriosclerosis que afecta el 40 al 50% de los casos. Esta incidencia ha sido confirmada por los hallazgos patológicos del Hospital Municipal de San Juan, el Hospital de Distrito de Ponce y el Registro de Muertes del Departamento de Salud de Puerto Rico.

La segunda causa importante de enfermedad cardíaca en nuestra clínica y en el Hospital de Distrito de Ponce fue la hiperten-

sión que causa aproximadamente el 21% de los casos. En las clínicas cardiológicas de Mayagüez y Arecibo la segunda causa importante de enfermedad cardíaca fue los defectos congénitos del corazón que causaron de un 22 al 32% de los casos estudiados.

El tercer y cuarto tipo importante de enfermedad del corazón en nuestra clínica y en la clínica del Hospital de Distrito de Ponce fueron los reumáticos y los congénitos, cada categoría produciendo aproximadamente 11 y 16% del total en estas dos clínicas respectivamente. En las clínicas de Mayagüez y de Arecibo el tercer y cuarto tipo de enfermedad cardíaca fueron los reumáticos e hipertensos. En la serie de autopsias de nuestro hospital (y la del Hospital de Distrito de Ponce); enfermedad congénita del corazón (18.8%) fue la segunda en importancia; la hipertensión (10.45%) fue tercera y los reumáticos (7.89%) fueron cuartos en importancia.

La quinta causa importante de enfermedad del corazón tanto en nuestro material clínico (3.2%) como en el material patológico (.62%) fue la sífilis del corazón. Este tipo de enfermedad del corazón también fue la quinta causa en importancia en todas las otras clínicas de la isla tanto en el material clínico como en el material patológico estudiado (Hospital de Distrito de Ponce).

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## EL "COUNTERSHOCK" EN EL TRATAMIENTO DE LA TAQUICARDIA PAROXISTICA VENTRICULAR\*

JOSE R. PASSALACQUA, M.D.

El uso de corriente eléctrica para terminar las arritmias cardíacas no es nuevo. Hace doscientos años Abilgaard<sup>1</sup> aplicó con éxito una corriente eléctrica directamente al corazón de un perro con fibrilación ventricular. Sin embargo, como suele ocurrir con los grandes descubrimientos, no se hizo uso clínico de este hallazgo hasta hace dieciséis años, cuando C. S. Beck<sup>2</sup> corrigió una fibrilación ventricular de larga duración por medio de la corriente eléctrica.

En la última década se ha venido aplicando el "countershock" eléctrico internamente, esto es, sobre el corazón expuesto por medio de la toracotomía, con éxito en muchos casos. Este método, sin embargo, requiere acceso inmediato a las facilidades de la sala de operaciones, y ha de llevarse a cabo en pocos minutos. El paro cardíaco ha sido tratado con marca-ritmos ("pacemakers") por este método heróico de la toracotomía.

Más recientemente P. Zoll<sup>3</sup> y su grupo han desarrollado el uso del marca-ritmo externo ("external pacemaker") en casos de paro ventricular, y el uso de la descarga eléctrica externa en la fibrilación ventricular.

Hacia fines del año 1961, Sidney Alexander, del Hospital Peter Bent Brigham, reportó lo que parece ser el primer caso de taquicardia paroxística ventricular tratado con descarga eléctrica aplicada externamente. Antes de recurrir al método él había aplicado al paciente grandes cantidades de amido-procaina ("Pronestyl"). Aunque la descarga eléctrica tuvo éxito en corregir la taquicardia paroxística, la depresión del miocardio causada por el exceso de Pronestyl mantuvo al paciente en estado de shock, descompensado y sin mejoría subjetiva durante varios días.

Tres meses después este mismo paciente se encontraba de vacaciones en la Florida cuando volvió a desarrollar taquicardia paroxística ventricular. Despues de unas dosis moderadas de Pronestyl y quinidina administradas sin éxito, fue trasladado en avión a Boston al Hospital Peter Bent Brigham. Esta vez el Dr. Alexander se cuidó de no administrar más Pronestyl ni quinidina que las dosis moderadas ya aplicadas en la Florida, y sometió al paciente inmediatamente a la descarga eléctrica. A los dos o tres

\* Este trabajo fue presentado en la reunión anual de la Asociación Puerto-riqueña del Corazón, en mayo de 1963, y también en la reunión anual de la Asociación Médica de Puerto Rico, en noviembre de 1963.

minutos, aquél despertaba de la ligera anestesia, su presión era de 130/60 y decía sentirse bien. El Dr. Alexander atribuye esta pronta recuperación al hecho de que esta vez no utilizó dosis altas y repetidas de drogas depresoras del miocardio como en la primera ocasión.

En la Revista de la Asociación Médica Americana del 25 de agosto de 1962, J. P. Crehan<sup>4</sup>, de Boston, informa otro caso de taquicardia paroxística ventricular tratado con descarga eléctrica. En marzo 30 de 1963, en la misma revista, Blumenthal<sup>5</sup> de Minneapolis informa otro caso. Otros casos han sido reportados durante el resto de este año de 1963.

A continuación presentamos un caso de taquicardia paroxística ventricular que fue sometido siete veces a descarga eléctrica durante este año.

#### Resumen del caso:

Un varón de setenta y seis años de edad fue llevado a la Sala de Emergencia del Hospital Auxilio Mutuo a las 9:00 P.M., el 5 de marzo de 1963, en estado de shock, sin presión arterial obtenible y con frecuencia cardíaca de 160 obtenida por auscultación. Una hora antes le había comenzado dolor intenso repentino en la región esternal seguido de palidez, sudoración y estado de shock. Tenía historial de haber sufrido una trombosis coronaria en 1956.

El médico residente le administró 1/4 de grano de sulfato de morfina para el dolor en el pecho. Con infusión de levarterenol la presión se elevó a 90/60. El electrocardiograma reveló taquicardia ventricular a una frecuencia de 160 por minuto.

Durante las siguientes veinticuatro horas se le administraron 2 Gms. de amido-procaina (Pronestyl): 550 Mgs. por inyección lenta endovenosa y 1,450 mgs. en infusión endovenosa de glucosa en agua. Se le aplicaron repetidas dosis de 50 Mgs. de Demerol para el dolor y se le colocó en cámara de oxígeno. La presión arterial logró mantenerse alrededor de 100/60 con el vasopresor (Levofed).

Once horas después del comienzo el conteo de glóbulos blancos era de 15,800 con 82% de neutrófilos. La transaminasa oxaloacética era 58 unidades; la dehidrogenasa láctica, 480 unidades.

La taquicardia ventricular persistía a la misma frecuencia de 160. El paciente estaba semi-inconsciente, pálido, cianótico y sudoroso. Era evidente que perdía terreno rápidamente. En este momento, 24 horas después del comienzo, se le aplicó sobre el precordio, con un electrodo sobre el manubrium y otro sobre el vértice del corazón una descarga de corriente alterna de 480 voltios durante 0.25 segundos, bajo anestesia general ligera. Esta consis-

tió en tiopental sódico y gas nitroso. Se añadió cloruro de succinilcolina para relajación muscular. Es importante la succinilcolina para evitar un estremecimiento muy severo durante la descarga. El ritmo convirtió inmediatamente a sinusal, con frecuencia de 86 a 90 por minuto. La presión arterial se elevó a 119/70 sin necesidad de levarterenol. El trazado electrocardiográfico ahora reveló ritmo sinusal normal y evidencia de un infarto antiguo de cara diafragmática para el cual habíamos tratado al paciente siete años antes. No había evidencia de isquemia reciente.

Hora y media después de la descarga recurrió la taquicardia ventricular y el paciente cayó de nuevo en estado de shock. Diez horas después del comienzo de este nuevo episodio, se aplicó otra descarga eléctrica bajo anestesia general ligera como anteriormente. Esta vez sólo usamos 200 voltios por 0.25 segundos, pero este voltaje no alteró la taquicardia. Enseguida usamos 480 voltios con lo cual revirtió el ritmo a lo normal con una frecuencia de 86 por minuto. De nuevo el paciente recobró el color normal rápidamente y su estado general mejoró en forma dramática.

Después de esta segunda descarga el electrocardiograma tampoco reveló enfermedad isquémica reciente del corazón. A las 36 horas del comienzo de dolor y taquicardia las transaminasas fueron como sigue: oxaloacética, 116 unidades; dehidrogenasa láctica, 810 unidades; transaminasa pirúvica, 14 unidades.

Opinamos que el paciente había tenido un infarto del miocardio y que la arritmia era su complicación, y comenzamos el tratamiento anticoagulante con heparina y Coumadin.

Al tercer día de enfermedad el electrocardiograma se hizo sugestivo de infarto sub-endocárdico y los trazados subsiguientes mostraron descenso del segmento ST hasta de 4 mms en las derivaciones izquierdas, substanciando así el diagnóstico de infarto. En ese tercer día el paciente desarrolló hipertermia de 102.2°F, taquicardia sinusal de 108, 32 respiraciones por minuto y expectoración hemoptóica. La presión arterial era de 140/90, y la auscultación revelaba estertores húmedos en el hemitorax derecho. El estudio radiológico mostró bronconeumonía derecha. Se le comenzó tratamiento intensivo con antibióticos: 400,000 unidades de penicilina cristalina potásica cada 3 horas e infusión continua intravenosa de tetraciclina a razón de 0.5 Gms. cada 8 horas. En la noche de ese tercer día la temperatura se elevó a 104°F. El paciente estaba en estado de confusión, desorientado, muy disnéico y la expectoración seguía siendo sanguinolenta.

En la mañana del cuarto día del ingreso, siendo la temperatura de 105°F debido a la bronconeumonía, volvió a presentarse la taquicardia paroxística ventricular. La situación entonces era como sigue: teníamos un paciente de 76 años de edad, con bronco-

neumonía, temperatura de 105°F, escalofríos intensos, infarto del miocardio y taquicardia paroxística ventricular. El aspecto general del paciente era tan "in extremis", que los familiares se opusieron a otra descarga eléctrica.

Optamos de nuevo por el Pronestyl, 250 mgs. por vía intramuscular, y prescribimos quinidina 0.40 gms. cada 2 horas, por 6 dosis. Cuando ya llevaba 2 Gms. de quinidina en el espacio de 10 horas, la condición del paciente parecía peor que nunca y la taquicardia persistía. En dos ocasiones durante esas 10 horas el paciente cayó en shock profundo sin pulso ni presión arterial obtenibles. Descontinuamos la quinidina y comenzamos la digitalización con Cedilanid.

Debemos señalar que en esas 10 horas críticas, bajo la terapia intensiva de penicilina y tetraciclina descrita, la temperatura descendió por crisis de 105 F que era a las 8:00 P.M., a 99 F a la mañana siguiente. Tuvimos la impresión que este descenso rápido y marcado en la temperatura contribuyó al estado de shock. A las 8:00 A.M. de ese quinto día la taquicardia ventricular cedió, esta vez sin descarga eléctrica, después de haber persistido durante 21 horas. Pensando que el digital pudo haber contribuido a este efecto le administramos otra dosis de 0.4 mg. de Cedilanid para completar 1.2 mgs. Esta vez el paciente estuvo libre de taquicardia por unas 27 horas, para caer de nuevo en shock con taquicardia paroxística ventricular. Otra dosis de Cedilanid de 0.4 mg. fue inefectiva. Ya para entonces la condición del paciente era sumamente crítica: pálido, cianótico, con disnea y en shock, rápidamente se consumía. La taquicardia ventricular secundaria al infarto subendocárdico persistía, así como la bronconeumonía, aunque ya la hipertemia había cedido.

Dadas las condiciones del paciente, los familiares se seguían oponiendo a otra descarga eléctrica. Optamos de nuevo por el Pronestyl, 2 Gms. disueltos en 20 cc. de glucosa en agua al 5%, administrados lentamente por vena, a razón de 100 mgs. cada dos minutos. Cuando ya había recibido 1000 mgs. el paciente se agravó, aumentando su estado de shock. El pulso se hizo filiforme.

Descontinuamos inmediatamente la droga. La crisis causada por ella duró unos 10 minutos. La taquicardia ventricular paroxística, sin embargo, persistía y por su parte seguía minando la condición del paciente. En este momento estábamos desorientados en cuanto a terapia ya que los familiares no permitían otra descarga eléctrica y nosotros temíamos al Pronestyl. El Isuprel sublingual fue inefectivo.

El consentimiento familiar vino a las pocas horas y de nuevo sometimos al paciente a descarga eléctrica de 480 voltios, por 0.25 segundo bajo anestesia muy ligera. La conversión al ritmo si-

nusal normal fue inmediata; el paciente recobró enseguida su buen color; el pulso se hizo de 88 por minuto y la presión arterial 140/60. Persistió este ritmo sinusal por 9 horas, al cabo de los cuales, en el séptimo día de enfermedad, de nuevo cayó el paciente con taquicardia paroxística ventricular, por cuarta vez. Esta vez le administramos 1,750 Mgs. de Pronestyl por vía oral e intramuscular sin resultado.

Otra descarga eléctrica con el mismo voltaje y espacio de tiempo de antes, aplicada 8 horas después de comenzada la taquicardia, volvió a convertir el ritmo a lo normal. Esta vez el paciente estuvo libre de taquicardia paroxística ventricular por 16 días, durante los cuales se le administraba sulfato de quinidina, 0.40 gmo. cada 8 horas. Al cabo de este tiempo de nuevo se quejó de dolor en el pecho y cayó en shock con taquicardia paroxística ventricular.

No respondió a tratamiento medicamentoso y, a las 14 horas de taquicardia, se le aplicó de nuevo la descarga con los mismos buenos resultados. La dosis de quinidina se elevó otra vez a 0.40 gms. cada 6 horas, dosis que se continuó hasta que el paciente fue dado de alta 25 días después.

Ya en su casa se continuó el tratamiento con anticoagulantes y se descontinuó la quinidina en vista de que ya transcurría casi un mes sin taquicardia.

Tres días después del alta del hospital, el 26 de abril de 1963, de nuevo le sobrevino dolor en el pecho y taquicardia paroxística ventricular. Fué hospitalizado de nuevo y se le aplicó descarga eléctrica, esta vez de corriente directa en vez de alterna. Recobró prontamente de la taquicardia ventricular y del estado de shock.

Esta vez las transaminasas permanecieron normales. El electrocardiograma no reveló infarto reciente. Aparentemente el dolor se debió a isquemia miocárdica secundaria a la taquicardia. Fue dado de alta al tercer día y se le mantuvo en quinidina, 0.40 gms. cuatro veces al día, dosis que le conservamos durante tres meses, reduciéndola entonces a 0.40 gms. tres veces al día. A las tres semanas de comenzada esta dosificación menor, en agosto de 1963, recurrió de nuevo la taquicardia paroxística ventricular. De nuevo la descarga con corriente directa trajo la conversión inmediata al ritmo normal.

El electrocardiograma y las transaminasas no mostraron infarto reciente.

Han transcurrido 3 meses desde el último episodio. El paciente ya ha reanudado buena parte de sus ocupaciones. Continúa recibiendo sulfato de quinidina en dosis de 0.40 Gmo. cuatro veces al día.

## COMENTARIOS

Hemos presentado un caso en el cual ocurrieron siete paroxismos persistentes de taquicardia paroxística ventricular rebeldes a tratamiento medicamentoso. En las siete ocasiones la descarga eléctrica corrigió pronta y eficazmente los paroxismos.

El método es razonablemente seguro ya que sus complicaciones poco frecuentes, la fibrilación auricular y el paro cardíaco, suelen responder a otra descarga eléctrica en el caso de la primera y a la acción del marca-ritmo en el caso del segundo.

Debemos mencionar en este momento que con el uso de la corriente directa en vez de alterna se suele evitar que ocurra la fibrilación ventricular después de la descarga. Después de su trabajo en perros con ritmo sinusal normal, Bernard Lown<sup>6</sup> concluye que con la corriente alterna hay una probabilidad en cinco de provocar fibrilación ventricular, riesgo que es casi no existente con la corriente directa.

Lown encuentra que las descargas que coincidan con la fase del período refractario que corresponde a la onda T del electrocardiograma, llamado "período vulnerable", suelen provocar fibrilación ventricular. Cada uno de los 30 perros que recibieron la descarga durante este período presentaron fibrilación ventricular, mientras que esta arritmia no ocurrió en ninguno de los 55 perros que recibieron la descarga fuera de este período vulnerable. Como es sabido, los más recientes defibriladores están sincronizados para producir la descarga al inscribirse el vértice de la onda R del electrocardiograma.

El sexto y séptimo tratamientos en el presente caso se llevaron a cabo con corriente directa y utilizando un defibrilador así sincronizado, evitando el período vulnerable. Sin embargo debemos señalar que ni en estos dos casos, ni en los primeros cinco cuando utilizamos corriente alterna no sincronizada, obtuvimos fibrilación ventricular ni paro cardíaco.

De los casos revisados en la literatura médica en inglés, sólo se reporta una muerte. Fue un paciente de 79 años de edad con taquicardia paroxística ventricular, que padecía además insuficiencia cardiaca congestiva, patología renal severa, y daño vascular cerebral. En este caso la descarga eléctrica produjo paro ventricular que no respondió al estímulo del marca-ritmo externo y otros métodos de resucitación.

Los voltajes bajos son más propensos a causar fibrilación ventricular. Suelen ser además inefectivos. El voltaje recomendado es de 450 voltios o más.

Debemos recordar que la quinidina y el Pronestyl, drogas valiosas, suelen ser también depresoras del miocardio y por tanto, po-

tencialmente peligrosas. Usadas en dosis altas pueden producir decompensación aguda del corazón que a su vez puede persistir después de la corrección de la arritmia con la descarga eléctrica.

Estudios hemodinámicos demuestran que el débito cardiaco, el volumen sistólico y la presión arterial, disminuyen en forma mínima después de la descarga mientras que la disminución es substancial con la quinidina, el Pronestyl y la Antazolina.

Es posible que estemos en duda sobre si se trata o no de una taquicardia ventricular. Por ejemplo, una taquicardia supraventricular acompañada de bloqueo de rama, puede simular, como es bien sabido, la configuración electrocardiográfica de la taquicardia ventricular. La distinción, sin embargo, resulta académica, o por lo menos, el error sería sin consecuencias, ya que la descarga eléctrica es capaz de terminar las taquicardias supraventriculares al igual que las ventriculares. Y, dicho sea de paso, también termina la fibrilación auricular al igual que la ventricular, de manera que estas arritmias serias, son hoy amenas al tratamiento.

Quisiéramos comentar sobre la elevación en las transaminasas observada en este caso. Treinta y seis horas después del dolor original y comienzo de la taquicardia, y doce horas después de la primera descarga las transaminasas tuvieron una elevación significativa, sin embargo, los electrocardiogramas no revelaron isquemia. Pensamos entonces en la posibilidad de que la elevación en transaminasas pudiera deberse a la descarga eléctrica, esto es, a cambios metabólicos en el miocardio causado por la corriente eléctrica, en vista de que los electrocardiogramas eran negativos. Sin embargo, subsiguientemente la configuración electrocardiográfica de infarto subendocárdico se hizo evidente. Además cuando 7 semanas más tarde aplicamos la descarga para una recurrencia de la taquicardia, las transaminasas permanecieron normales. Parece lógico asentar, pues, que una elevación de las transaminasas después de la descarga eléctrica no es atribuible a este método de tratamiento sino que probablemente es debida a un infarto del miocardio.

¿Cuál es el mecanismo de acción de la descarga eléctrica en las arritmias mencionadas? Sydney Alexander, Lown, Zoll, y otros han postulado que la descarga eléctrica al depolarizar simultáneamente todas las fibras del miocardio, extingue los focos ectópicos y así le da una oportunidad al nódulo sinusal de recobrar su posición de marcador del ritmo.

### Ventajas del Método

El método es fácil de administrar bajo anestesia ligera. Los resultados suelen ser inmediatos y dramáticamente buenos. No

hay depresión de las funciones del miocardio, esto es, la contractilidad, ritmicidad y conductibilidad permanecen inalteradas. Es raro que haya efectos indeseables. Nosotros no los observamos en las siete aplicaciones que hicimos, a pesar del estado de shock, cianosis y toxicidad que a veces existía.

### Riesgos

Como ha quedado señalado, las complicaciones del método son la fibrilación ventricular y el paro ventricular, riesgos que generalmente responden a otra descarga eléctrica en el caso de la fibrilación, o al marca-ritmo en el caso del paro.

El tratamiento es doloroso y por ello requiere anestesia general.

### SUMMARY

We have presented the case of a 76 years old male who showed recurrent attacks of paroxysmal ventricular tachycardia following a subendocardial infarct. Quinidine and Pronestyl were ineffective in treatment. Electrical countershock, on the other hand, proved to be promptly and dramatically efficacious, even in moments of utmost crisis when the patient had complicating bronchopneumonia. Seven attacks occurred in all. The first 5 were corrected with alternating current countershock; the last 2 with direct current countershock the discharge being synchronized with the peak of the R wave of the electrocardiogram.

The feared complications of countershock, ventricular fibrillation and cardiac arrest, were not encountered in the 5 instances when alternating current was used or in the 2 instances when direct current was utilized.

The advantages of synchronized d.c. countershock versus a.c. countershock, as described in the literature, are discussed.

Countershock treatment has the advantage of being only slightly depressant to the myocardium as compared with quinidine or Pronestyl. It is usually promptly effective. Ventricular fibrillation and cardiac arrest, if they should occur following countershock, usually respond to another countershock or to the external pacemaker, respectively.

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## USE OF SODIUM D-THYROXINE IN EUTHYROID CORONARY SUBJECTS

### PRELIMINARY REPORT

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The association between a high dietary fat intake and human atherosclerosis has not been definitely established. However, there is substantial evidence that a high serum cholesterol is a predisposing factor in the development of coronary artery disease. For this reason, several attempts have been made during the last decade to lower serum cholesterol using dietary modifications and pharmaceutical agents designed to suppress the lipid metabolic derangement which is supposed to cause the pathologic process.

It has been known for many years that thyroid extract lowers serum cholesterol. Unfortunately, its hypermetabolic effect is particularly undesirable in the coronary subject. Recently, interest has been given to derivatives of thyroid hormone which lower serum cholesterol with relatively insignificant calorogenic activity.

Sodium D-Thyroxine, the sodium salt of 3, 5, 3', 5'-tetraiodo-D-Thyronine is one of these agents. It produces a hypocholesterolemic response comparable to that of L-Thyroxine with about one tenth of the calorogenic activity.

The availability of effective and well tolerated hypocholesterolemic drugs presents the opportunity to determine whether such therapy results in decrease of the morbidity and mortality of coronary artery disease. This is the ultimate purpose of the present investigation. However, an important preliminary step is the determination of the tolerance of known coronary subjects to a dose which is expected to produce an effective hypocholesterolemic response with minimal side effects. The present report concerns this aspect of treatment with D-Thyroxine as observed in the first 40 patients who have entered the study.

### MATERIALS AND METHODS

The patients were male veterans admitted to the San Patricio V. A. Hospital. Their ages ranged from 27 to 70 years with an

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average of 51 years. None of them had previously received hypocholesterolemic therapy. No attempt was made to select hypercholesterolemic individuals inasmuch as it was desired to investigate the applicability of this therapy to coronary patients as a whole. Only patients who had definite clinical evidence of coronary artery disease, either in the form of a well documented myocardial infarction or evidence of myocardial necrosis after a prolonged state of coronary insufficiency were accepted in the study.

The baseline examinations included a complete history and physical examination, EKG,  $I_{131}$  uptake, and Triiodothyronine (T3) uptake by RBC. The serum cholesterol was determined according to the method of Zak tested<sup>1</sup> daily against standard controls. Beta-Lipoproteins were determined according to the immunocrit method.<sup>2</sup> Total serum fat was determined according to the method of Brandstein and Castellano.<sup>3</sup>

At the completion of the baseline examination all patients were randomized using an envelope method into either a D-Thyroxine or a placebo group. A double blind design was used to prevent any possible bias. As all patients had known coronary artery disease, a conservative dose of 4 mgm. per day of D-Thyroxine was used in the drug treated group in order to avoid the possibility of hypermetabolic hazard.

All patients were urged to follow their customary dietary programs. Previous cardiovascular therapy was continued without any modification. Patients were seen at a special clinic every three months where the indicated follow-up examinations were performed.

At the end of one year of therapy the available data was tabulated and examined statistically by an independent party without breaking the double blind code. Differences of probability at levels less than  $p = <.05$  were considered significant. In all tables N represents the number of patients in the particular group.

At the end of three months of treatment eighteen patients on D-Thyroxine showed an average fall in serum cholesterol of 24.011 mgm.%. The change is statistically significant. Twenty two patients on placebo during the same period showed a fall in serum cholesterol of 13.40 mgm.%. This change is not quite significant at the chosen level of probability.

After six months of treatment 16 patients receiving D-Thyroxine showed a questionably significant fall in serum cholesterol ( $p < .1$ ) while 20 patients on placebo did not show a significant fall in serum cholesterol ( $p < .1$ ) while 20 patients on placebo did not show a significant fall. After a year of therapy eleven patients on D-Thyroxine had a fall in serum cholesterol of 10.95 mgm. %, and 13 patients on placebo had an increase in serum cholesterol of

SERUM CHOLESTEROL RESPONSES

Initial level	Thyroxine		Placebo	
	N	Diff. (mgm. %)	N	Diff. (mgm. %)
3 mo.	18	-24.01	22	-13.4
S.E.		10.95		6.56
p		<.05		<.1
p		N.S.		
-----				
6 mo.	16	-21.537	20	-7.39
S.E.		10.41		8.197
p		<.1		N.S.
p		N.S.		
-----				
1 year	11	-10.95	13	+2.18
S.E.		13.14		9.64
p		N.S.		N.S.
p		N.S.		

## RESULTS

## Serum Cholesterol: (Tab. 1)

2.18 mgm. %. Neither change is statistically significant. Comparison of the differences at all treatment levels does not show a

BETA-L RESPONSES

Initial level	D-Thyroxine		Placebo	
	N	Difference	N	Difference
3 mo.	18	.044	22	.0409
S.E.		.137		.1412
p		N.S.		N.S.
p		N.S.		
-----				
6 mo.	16	.0187	20	.205
S.E.		.1824		.1177
p		N.S.		N.S.
p		N.S.		
-----				
1 Year	11	.2818	13	.4846
S.E.		.196		.1526
p		N.S.		<.01
p		N.S.		

## Beta-Lipoproteins: (Tab. 2)

significant preference for either the D-Thyroxine or the placebo regime.

A fall in serum cholesterol in the D-Thyroxine group was noted at three months in 66.66% of the patients and approximately the same percentage persisted throughout the year. In the placebo group a fall in serum cholesterol occurred in 68.18% of the patients at three months but this decreased to 38.46% at one year. In the D-Thyroxine group the average fall in serum cholesterol was about 11% of the control value throughout the year, while in the placebo group the average fall was 6.49% at three months and there was an increase of 1.03% at one year.

No significant change was shown by either the D-Thyroxine or the placebo groups at three and six months. At the end of a year there was a significant elevation in Beta-Lipoproteins in 13 patients on placebo, while in the 11 patients receiving D-Thyroxine there was no similar change. However, the difference between these differences is not significant.

#### TOTAL SERUM FAT RESPONSES

	D-Thyroxine		Placebo	
	N	Difference	N	Difference
Initial level		472.29 mgm. %		525.98 mgm. %
1 Year	10	+74.77	9	+59.47
S.E.		57.9		104.76
p		N.S.		N.S.
p			N.S	

#### Total Serum Fat: (Tab. 3)

No significant change was observed in total serum fat in either the D-Thyroxine or placebo groups at the end of one year.

#### I<sub>131</sub> THYROID UPTAKE

	D-Thyroxine		Placebo	
	N	Difference	N	Difference
Initial level		15.35%		17.76%
1 Year	7	-6.285	7	+7.28
S.E.		3.34		2.8
p		N.S.		<.05
p		<.01		

#### I<sub>131</sub> Uptake: (Tab. 4)

Thirteen patients on placebo showed an increase in  $I_{131}$  uptake of +7.28% after one year. This represents a significant elevation ( $p < .05$ ). In seven patients receiving D-Thyroxine, the  $I_{131}$  uptake decreased by -6.285%. The latter change is not significant, but comparison of both differences shows a significant difference between the D-Thyroxine and placebo regimes ( $p < .01$ ). This indicates that D-Thyroxine produces a significant decrease in the  $I_{131}$  uptake by the thyroid gland.

Initial Uptake	$T_3$ RBC UPTAKE			
	D-Thyroxine		Placebo	
		13.38%		13.978%
3 mo.	N	Difference	N	Difference
3 mo.	15	+2.946	14	+.51
S.E.		.767		.54
p		<.01		N.S.
p		<.05		
-----				
6 mo.	N	Difference	N	Difference
6 mo.	13	+2.446	16	+.675
S.E.		.85		.903
p		<.05		N.S.
p		N.S.		
-----				
1 Year	N	Difference	N	Difference
1 Year	10	+4.31	7	+.1285
S.E.		1.39		.79
p		<.02		N.S.
p		<.05		

#### Tri-Iodothyronine ( $T_3$ ) RBC uptake: (Tab. 5)

Patients on D-Thyroxine showed a significant increase in the  $T_3$  uptake by RBC's. Patients on placebo did not show a significant increase. Comparison of the differences indicates that a significant effect is present at three and nine months ( $p < .05$ ).

#### SIDE EFFECTS

At this stage of the investigation changes in severity, duration, and frequency of anginal attacks have not been significantly different in the placebo and D-Thyroxine groups, (Tab. 6). The nitroglycerine requirement is also approximately the same in both groups. No increase in calorogenic side effects has been observed in the D-Thyroxine as compared with the placebo group, (Tab. 7), nor has there been any significant body weight difference.

#### Effects on clinical manifestations of atherosclerosis:

Up to the present time the number of atherosclerotic com-

A N G I N A  
D-Thyroxine (14 cases)

	Better	Same	Worse
Duration	4 (28.6%)	8 (57.2%)	2 (14.3%)
Frequency	2 (14.3%)	10 (71.5%)	2 (14.3%)
Severity	2 (14.3%)	10 (71.5%)	2 (14.3%)
Average	19.0%	66.7%	14.3%

-----  
Placebo (14 cases)

	Better	Same	Worse
Duration	6 (42.9%)	6 (42.9%)	2 (14.3%)
Frequency	6 (42.9%)	5 (35.7%)	3 (21.4%)
Severity	5 (35.7%)	8 (57.2%)	1 (7.15%)
Average	40.5%	45.2%	14.3%

S I D E   E F F E C T S

(INCREASE)

	Diarrhea	Appetite	Sweating	Nervousness	Tachycardia & Palpitation
D-THYROXINE (19 pts.)	0%	21.1%	0%	0%	42.1%
PLACEBO (22 pts.)	4.5%	22.8%	0%	4.5%	35.4%

lications in both treated and untreated groups has not been sufficiently great to justify breaking the code. To date one patient has developed a myocardial infarction, another one had a severe episode of coronary insufficiency and two more developed atherosclerotic occlusions of a major peripheral artery. The incidence of atherosclerotic complications will be the subject of a future report.

DISCUSSION

The hypocholesterolemic effect of D-Thyroxine has been documented in numerous published studies. The present investigation likewise has revealed a significant hypocholesterolemic response in unselected euthyroid coronary subjects 3 months after

treatment with 4 mgm. per day of D-Thyroxine. However, the rather pronounced though not quite significant hypocholesterolemic response noted in our placebo treated patients qualifies the interpretation of the effect noted in the D-Thyroxine group.

At the present time we are not able to explain the suggestive hypocholesterolemic response in the placebo group. A similar effect was noted in another D-Thyroxine study controlled with placebos,<sup>4</sup> but most investigators have not noted this response.<sup>5,6,7,8</sup>

Tension, physical discomfort, and fear have been reported to elevate serum cholesterol in humans.<sup>9,10</sup> Considerable anxiety incident to their known coronary disease was probably present in our subjects. Therefore, it may be possible that the relief of tension by the reassurance of close medical supervision may have lowered the serum cholesterol previously elevated by the stress of anxiety in our placebo treated patients. It is apparent that this finding requires further elucidation because it may be of importance in the interpretation of hypocholesterolemic responses in this type of subjects.

Compared to other studies, the hypocholesterolemic effect that we have observed is relatively small. This may be due in part to our deliberate use of a relatively small dose of D-Thyroxine. In other studies doses as high as 12 and even 16 mgm. per day have been used, but with these higher doses the hypermetabolic effect may be hazardous in coronary patients.

Another reason for the relatively minor hypocholesterolemic response may be that we did not select hypercholesterolemic subjects. Other studies have shown that D-Thyroxine has a greater effect when the serum cholesterol is high. When our D-Thyroxine patients are classified according to the initial serum cholesterol it may be seen that those with the highest initial level exhibit the greatest response, (Tab. 8). This is also true in the placebo group. However, the individual responses were much more striking in the D-Thyroxine treated patients. In comparison the hypocholesterolemic response in the placebo group was relatively uniform throughout.

These observations may be of importance in considering the applicability of hypocholesterolemic therapy to coronary subjects as a whole. Perhaps certain initial levels of serum cholesterol and individual responsiveness are prerequisites for successful hypocholesterolemic therapy.

Under the conditions of the present study we have been unable to detect any effect of D-Thyroxine in lipid fractions other than serum cholesterol. In general this agrees with published reports. However, a decrease in elevated low density lipoproteins after therapy with D-Thyroxine has been reported.<sup>11</sup>

Our results regarding changes in the  $I_{131}$  uptake by the thy-

D - T H Y R O X I N E

Range	N	Mean Initial Chol.	Mean 3 Mo. Chol.	Change Mgm.	Change %
> 225	6	250.05	212.38	-37.66	-15.06%
225-175	8	205.48	171.61	-33.88	-16.4%
< 175	4	163.42	179.62	+16.2	+9.91%

P L A C E B O

Range	N	Mean Initial Chol.	Mean 3 Mo. Chol.	Change Mgm.	Change %
> 225	7	262.62	224.45	-38.17	-14.53%
225-175	10	198.67	197.16	-2.51	-1.26%
< 175	5	142.9	142.4	- .15	- .35%

roid gland induced with D-Thyroxine are similar to those reported by other authors.<sup>8</sup> It has been suggested that this indicates a suppression of TSH.<sup>12</sup> It is possible that the minor calorogenic effect of D-Thyroxine may be in part offset by decrease in endogenous thyroid secretion secondary to TSH suppression. The significance of this effect in long term hypcholesterolemic therapy with D-Thyroxine requires additional observation.

Increase in the RBC uptake of  $T_3$  in our patients was fairly consistent. The change was highly significant statistically. This is interpreted to indicate that D-Thyroxine binds with the same proteins which also transport thyroid hormone and triiodothyronine.

The tolerance of our known coronary patients to D-Thyroxine at a dosage level of 4 mgm. per day has been excellent. It may be possible that no appreciable increase in side effects may occur with some increment in dosage, and that a more effective hypcholesterolemic response may be obtained thereby. This study will be continued along this line of thought in order to attempt to determine if hypcholesterolemic therapy has an effect on the morbidity and mortality of coronary artery disease.

## SUMMARY

The preliminary experience in the use of D-Thyroxine under a double blind design in 40 coronary patients is presented.

A significant but relatively small hypcholesterolemic response was observed in the D-Thyroxine treated patients. The interpre-

tation of this change is difficult because patients treated with placebo also showed a not quite significant hypocholesterolemic effect. It is suggested that this may have been due to the reassuring factors associated with placebo therapy in stressed subjects.

The hypocholesterolemic response in both treated and placebo groups was more marked in those subjects with the highest initial serum cholesterol level, suggesting that the latter maybe a prerequisite to effective therapy.

No significant changes in Beta-lipoproteins or total serum fat were observed but there was a significant decrease in  $I_{131}$  thyroid gland uptake and a significant increase in RBC uptake of  $T_3$  after D-Thyroxine therapy.

No significant side effects were noted at the dose level of 4 mgm. per day of D-Thyroxine that was used. It is believed that at this or perhaps slightly greater dosage, the drug lends itself for investigation to attempt to determine if hypocholesterolemic therapy has an effect in the morbidity and mortality of coronary artery disease.

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## EDITORIAL

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### DIET AND CORONARY HEART DISEASE

In about 90% of the cases atherosclerosis is the underlying cause of coronary heart disease. The genesis of atherosclerosis remains obscure and controversial.

The predisposing and contributing factors are age and sex, heredity, body build, arterial hypertension, diabetes, mellitus, myxedema, familial hypercholesterolemia, diseases of the biliary tract, polycythemia, obesity, smoking, temperament, occupation, and ethnic, geographic and dietary factors.

The metabolic theory of atherosclerosis is today the most popular. Disturbances of lipid metabolism, and more specifically in the metabolism of cholesterol have outranked all other theories. Socioeconomic and dietary surveys as well as experimental and clinical evidences seem to point to their validity. The impact played by cholesterol and its metabolism, by Barr's beta lipoproteins and Gofman's Svedberg units on the minds of both physicians and laity has been strong, often confusing and frequently overestimated.

Ancel Keys has conducted the most complete and reliable epidemiological and geographic survey bearing on the relationship between dietary fat intake and the frequency of coronary heart disease. His studies among low-income Spaniards and Italians, Nigerians, Yemenite Jews, and Guatemalan Indians seem to substantiate the idea that the low incidence of coronary disease in these populations estimated to be one-fourth that of the North Americans, English and Scandinavians may be attributed to the low fat content of their diet. Similar conclusion can be drawn from the studies of Kimura in Japan, and from those of Higginson among the South African Bantu. The lower mortality rate of coronary disease in the Scandinavian Countries during World War II was similarly attributed by Björck to the enforced restriction of dietary fat.

Our experience in Puerto Rico seems to confirm the fact that coronary disease is seen predominantly in the upper socioeconomic classes and rarely in the poor or low-income groups. This difference has also been attributed to higher fat and protein consumption in the well-to-do people.

Other workers doubt the validity of the epidemiological and dietary surveys because they do not take into account socioeconomic and other environmental differences.

The more obvious of the environmental factors are climate, food and intraspecific relationship. Herbert L. Ratcliffe<sup>1</sup> from the

Penrose Research Laboratory, Zoological Society of Philadelphia claims that the frequency of coronary disease of recent decades cannot be attributed wholly to changes in dietary habits. "It may be related, he says, equally well to changes in intraspecific relationship." "Living standards for large segments of the population have improved as a result of continued industrial growth. There has ensued increased food intake, especially animal protein and fat, as well as rapid urbanization. Increases in population density, as well as in social and economic competition must be recognized as other environmental changes that accompany economic growth".

He concludes that "differences in the intensity of social and economic competition may more readily account for differences in the frequency of coronary arteriosclerosis among Japanese living in Japan, Hawaii and California than the levels of dietary fat".

In a dietary survey of a small number of Yemenite Jews who have lived in Israel for over 25 years as compared with recent immigrants and with Jews in the Yemen, Cohen<sup>2</sup> found that the main dietary difference was that carbohydrates consumed in the Yemen consisted of starches with very little, if any sugar, while in Israel, sucrose accounted for 25 to 30% of the total carbohydrate intake.

Both diabetes and atherosclerosis were more prevalent in the Yemenite Jews settled in Israel than in recent immigrants of the same race.

Cohen suggests that "it is possible that excessive ingestion of sucrose leads to a state of "relative insulin insufficiency" which, in turn, causes impaired metabolism of the vascular structures, and predisposes them to infiltration of lipids, and that the increased incidence of atherosclerosis and diabetes in Yemenites who have lived in Israel for many years may be attributed to excessive ingestion of sugar.

It may well be that the excessive consumption of sugar predisposes to diabetes and this in turn to atherosclerosis. Vascular accidents is the cause of death in 62% of diabetics, and coronary thrombosis in 22%. Mortality from myocardial infarction is twice as frequent in diabetic patients than in non-diabetics. Vascular lesions, nevertheless, are relatively rare in the diabetes of hemochromatosis.

It is also difficult to explain the elevation of blood cholesterol observed in coronary heart disease and its normal or about normal concentration in cerebral and peripheral vascular disease.

Analysis of food-balance data in the U.S. suggests that during the last 40 or 50 years the fat content of the American Diet has increased from about 30% of total calories in 1910 to more than 40% at present.

The mortality rate from coronary heart disease in men from 40 to 70 years of age is higher in the U. S. than in most countries. It has increased explosively from 7.9% per 100,000 population in 1930 to 226.1 per 100,000 in 1952.

The "National Diet - Heart Study", supported by the National Heart Institute and other Federal Agencies with the cooperation of the American Heart Association will consist of the study and observations of 100,000 healthy men of 45 to 54 years of age assigned to one of several diets for a period of 4 to 5 years. Leading food companies are cooperating in the preparation of diets meeting several sets of specifications involving changes in the type and amounts of saturated and polyunsaturated fats as well as cholesterol content.

This complicated and costly, long term, "double blind" study which has been tentatively initiated in Boston, Baltimore, Chicago, Minneapolis and Oakland proves that the possible relationship between diet and heart disease is far from being established.

We agree with Dack<sup>3</sup> that there are not, as yet, scientific basis for making drastic or revolutionary changes in the American diet, but present knowledge seems to justify the following therapeutic approaches:

1. In angina pectoris or coronary insufficiency, the meals should be small, bland and low in fat content. Four or five feedings should be given daily. Large heavy dinners, even the act of mastication, may provoke pain and a high fat meal may increase blood viscosity and coagulability because of postprandial lipemia.
2. In acute occlusion food should be withheld for the first few hours. Cracked ice, fruit juices, broth, cooked cereals, custard and milk are gradually added, so that within a few days the patient is receiving from 800 to 900 calories daily of a well balanced diet containing not over 20 gm. fat. The low calorie diet results in lowering of the basal metabolic rate as much as—20 to—30%, and in a decrease in pulse rate and cardiac work. In 2 or 3 weeks a more liberal diet of 1000 to 1200 calories is instituted and continued until the patient returns to moderate activity.
3. Persons who, because of heredity, hypercholesterolemia, mesomorphism, electrocardiographic abnormalities or other predisposing factors are considered prone to coronary attacks, should be given a low calorie and low fat diet. Fish and corn oil should make up the greater part of the fat intake.
4. We should remember that a diet lacking natural fats would diminish the necessary supply of vitamins A, D, E and K.

The motto for the physician should therefore continue to be: "Primum non nocere".

**Dr. Ramón M. Suárez**

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## SECCION DE RESUMENES

**PARGYLINE, CHEESE, AND ACUTE HYPERTENSION.** F. S. Glazener, M.D., William A. Morgan, M.D., John M. Simpson, M.D. and Paul K. Johnson, M.D. J.A.M.A. 188: 754-55, 1964.

The occurrence of the syndrome of "cheese hypertension" was first described in 1963 in patients receiving the MAO (Mono-amino oxidase) inhibitor tranylcypromine sulfate. This is a report of a severe, paradoxical hypertensive crisis occurring in a patient taking the antihypertensive MAO inhibitor, pargyline hydrochloride, apparently precipitated by the ingestion of aged cheddar cheese. The paroxysms, which mimic the discharge from a pheochromocytoma, are believed to be due to tissue accumulation of L-epinephrine and L-norepinephrine. Tyramine, one of the pressor amines found in cheese, may act as a pressor substance or it may provoke the release of stored catecholamines. In contrast to phaeochromocytoma, urinary excretion of 3 methoxy, 4-hydroxy mandelic acid has been reported as normal. The treatment of choice for the paroxysm is phentolamine methanesulfonate (Regitine). Physicians prescribing Pargyline should be aware of this complication and caution patients against eating ripened cheese.

M. MARTINEZ MALDONADO, M.D.

**PRESENT STATUS OF THROMBOLYTIC THERAPY.** Adam J. Johnson, M.D. Am. Heart, J. 67: 418-420, 1964.

The problems encountered in the use of thrombolytic drugs are discussed from three main points of view: 1) general biochemical problems, 2) effect of clot surface, and 3) age of clot. What these points emphasize is the inherent difficulties presented by these drugs, showing that solution of a clot is not simple in the living organism. Streptokinase (SK), an enzyme first discovered in 1933, and streptokinase containing thrombolytic agents are also discussed from their biological, chemical and physical characteristics. One of the most important aspects is the ease with which antibodies and inhibitors are produced against this medication. In spite of the problems presented by SK antibody and inhibitors, 24-to 72 hours infusions of SK have been shown to be thrombolytic under well controlled conditions. Determinations of prothrombin and fibrinogen serve to warn the individual when a serious bleeding defect may occur due to hyperplasminemia. Also determination of plasminogen and activator must be run during the infusion. The difficulty with which these determinations are made complicates the use of these agents. The similarity of Plasmin to SK is mentioned. Urokinase, which has become available only recently, is briefly discussed. It is mentioned that it seems to be of promising value. In all, even though these agents have been extensively studied, the true clinical usefulness of thrombolytic therapy must await appropriate, well-designed clinical trials.

M. MARTINEZ MALDONADO, M.D.

**SYNCOPE WITH COMPLETE HEART BLOCK - Differentiation of Real Simulated Adams-Stokes Seizures by Radiotelemetry.** Gordon H. Ira, M.D., Walter L. Floyd, M.D., and Edward S. Orgain, M.D., J.A.M.A. 188: 707-710, 1964.

Four patients with complete heart block were studied prior to implantation of a pacemaker for complete heart block, and their syncopal episodes monitored utilizing the radiotelemetry electrocardiographic tape system. This

permitted differentiation between four different mechanisms of syncope preventing that two patients, with mechanisms unrelated to heart block, be submitted to surgery. One patient was found to have a right atrial myxoma and one patient exhibited hyperventilation attacks. Patient number three had 3 types of attacks, all related to ventricular asystole, and the fourth patient had recurrent ventricular tachycardia-fibrillation. Thus, before implanting a pacemaker, a demonstration of the underlying cardiac mechanism seems mandatory. This can be done with confidence by the use of radiotelemetry.

M. MARTINEZ MALDONADO, M.D.

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**RE-EVALUATION OF THERAPY OF ACUTE MYOCARDIAL INFARCTION.**

**Malcolm I. Lindsay Jr., M.D., Ralph E. Spickerman, M.D. Am. Heart J. 67:559-564, 1964.**

In the form of a review the authors bring out the fact that in spite of the general advancement of medical technology, the rate of mortality from acute myocardial infarction has not declined significantly. Special attention is given to anticoagulant therapy, to the development of intensive care units, and to the use of fibrinolytic agents in the therapy of acute infarction. Four general principles seem to be well accepted in the therapy of acute infarction: (1) administration of oxygen and adequate analgesia while pain persists; (2) prompt treatment of associated hypotension or congestive heart failure; (3) physical rest for the heart; and (4) conscientious attention to the details of good general care. Anticoagulant therapy is used to prevent complications of intravascular or intracardiac thrombosis and of embolism. Although a decreased incidence of thromboembolic phenomena has been reported, there is also heavy criticism of routine anticoagulation. There is, in fact, doubt that this will reduce mortality from acute myocardial infarction. The authors present their review of 295 cases of myocardial infarctions admitted to the Mayo Clinic from 1945 through 1959. There were 355 infarctions; of these, 239 were treated with anticoagulants and 116 were not. Thromboembolic phenomena occurred in 3.3 per cent of the former group in contrast with 5.1 per cent in the latter. Although hemorrhage occurred in 3.8 per cent of the infarctions during the hospitalization period, there were no fatalities from this complication. Verified myocardial rupture occurred 24 hrs. or more after 1.7 per cent of the infarctions treated by anticoagulants and after 4.3 per cent of those not so treated. Death during the first 6 weeks resulted from 17.6 per cent of the 239 infarctions treated by anticoagulants and from 19.8 per cent of the 116 not so treated. Since this data show some success in decreasing mortality rate by anticoagulant therapy, the authors propose that further controlled studies be done. The authors believe that a significant decrease in deaths from acute myocardial infarction will result from prevention of so called "acute coronary failure". The mechanism in most instances is the development of ventricular fibrillation or other arrhythmias incompatible with adequate support of circulation. Today, these complications are potentially reversible if prompt recognition is followed by intense care. The use of closed chest cardiac massage, defibrillators or cardiac pacemakers by well trained people can help in these circumstances. The difficulties presented by the use of thrombolytic therapy are also discussed. Although new, this form of therapy may prove of help in decreasing the mortality and thromboembolic complications of acute myocardial infarction. To conclude, the authors call for further investigations of all these tools of therapy in acute myocardial infarction.

M. MARTINEZ MALDONADO, M.D.

## **PRINCIPLES OF MEDICAL ETHICS**

### **PREAMBLE**

These principles are intended to aid physicians individually and collectively in maintaining a high level of ethical conduct. They are not laws but standards by which a physician may determine the propriety of his conduct in his relationship with patients, with colleagues, with members of allied professions, and with the public.

### **SECTION 1**

The principal objective of the medical profession is to render service to humanity with full respect for the dignity of man. Physicians should merit the confidence of patients entrusted to their care, rendering to each a full measure of service and devotion.

### **SECTION 2**

Physicians should strive continually to improve medical knowledge and skill, and should make available to their patients and colleagues the benefits of their professional attainments.

### **SECTION 3**

A physician should practice a method of healing founded on a scientific basis; and he should not voluntarily associate professionally with anyone who violates this principle.

### **SECCION 4**

The medical profession should safeguard the public and itself against physicians deficient in moral character or professional competence. Physicians should observe all laws, uphold the dignity and honor of the profession and accept its self-imposed disciplines. They should expose, without hesitation, illegal or unethical conduct of fellow members of the profession.

### **SECTION 5**

A physician may choose whom he will serve. In an emergency, however, he should render service to the best of his ability. Having undertaken the care of a patient, he may not neglect him; and unless he has been discharged he may discontinue his services only after giving adequate notice. He should not solicit patients.

## **SECTION 6**

A physician should not dispose of his services under terms or conditions which tend to interfere with or impair the free and complete exercise of his medical judgment and skill or tend to cause a deterioration of the quality of medical care.

## **SECTION 7**

In the practice of medicine a physician should limit the source of his professional income to medical services actually rendered by him, or under his supervision, to his patients. His fee should be commensurate with the services rendered and the patient's ability to pay. He should neither pay nor receive a commission for referral of patients. Drugs, remedies or appliances may be dispensed or supplied by the physician provided it is in the best interests of the patient.

## **SECTION 8**

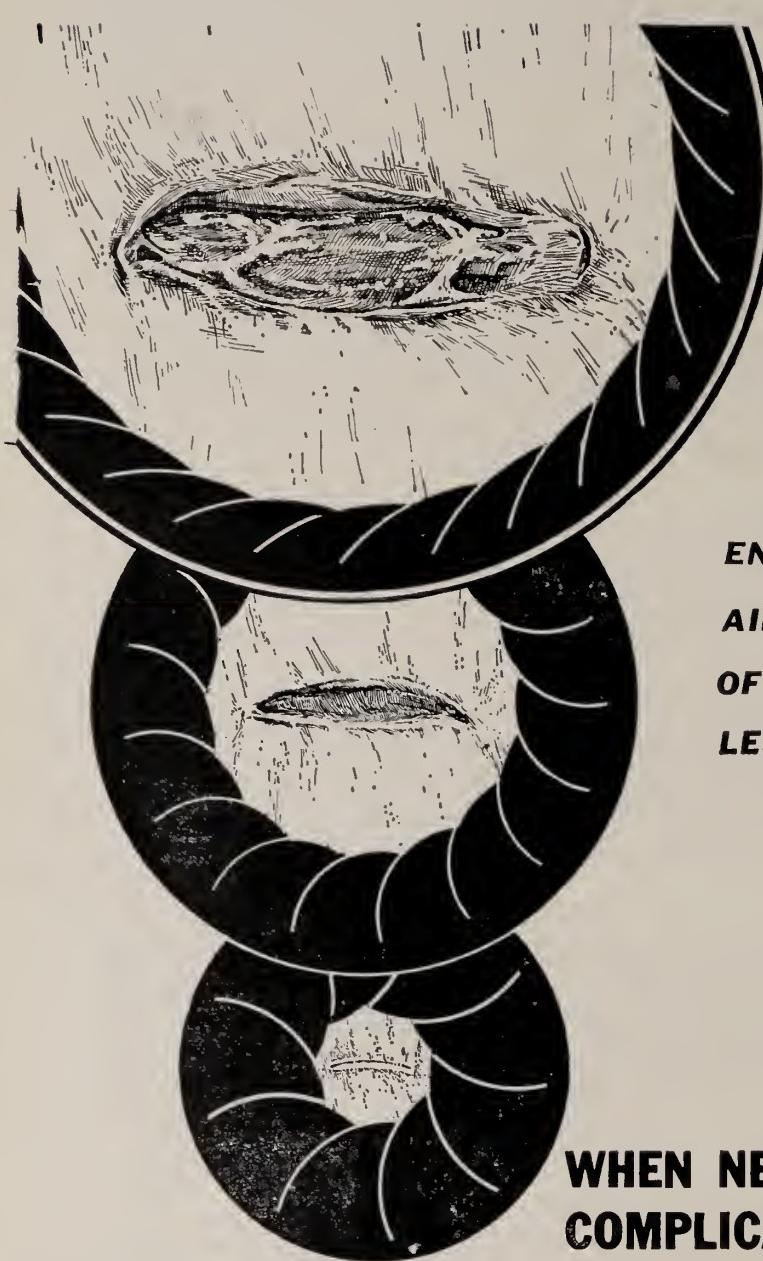
A physician should seek consultation upon request; in doubtful or difficult cases; or whenever it appears that the quality of medical service may be enhanced thereby.

## **SECTION 9**

A physician may not reveal the confidences entrusted to him in the course of medical attendance, or the deficiencies he may observe in the character of patients, unless he is required to do so by law or unless it becomes necessary in order to protect the welfare of the individual or of the community.

## **SECTION 10**

The honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual, but also to society where these responsibilities deserve his interest and participation in activities which have the purpose of improving both the health and the well-being of the individual and the community.

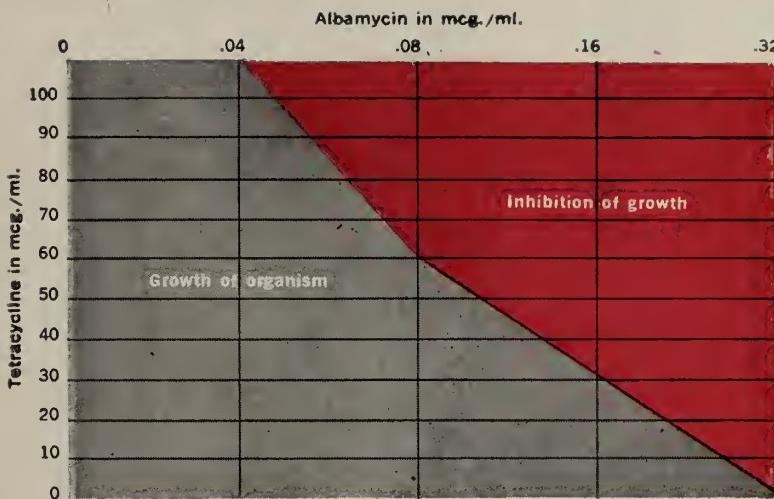


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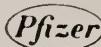
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# BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO

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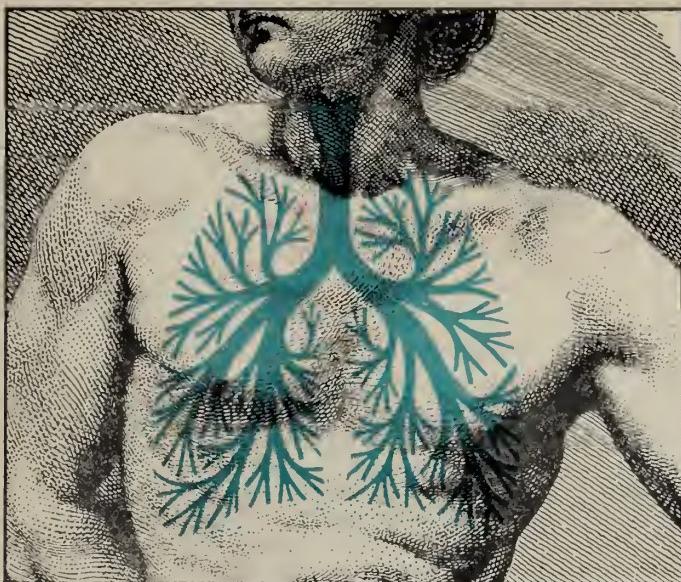
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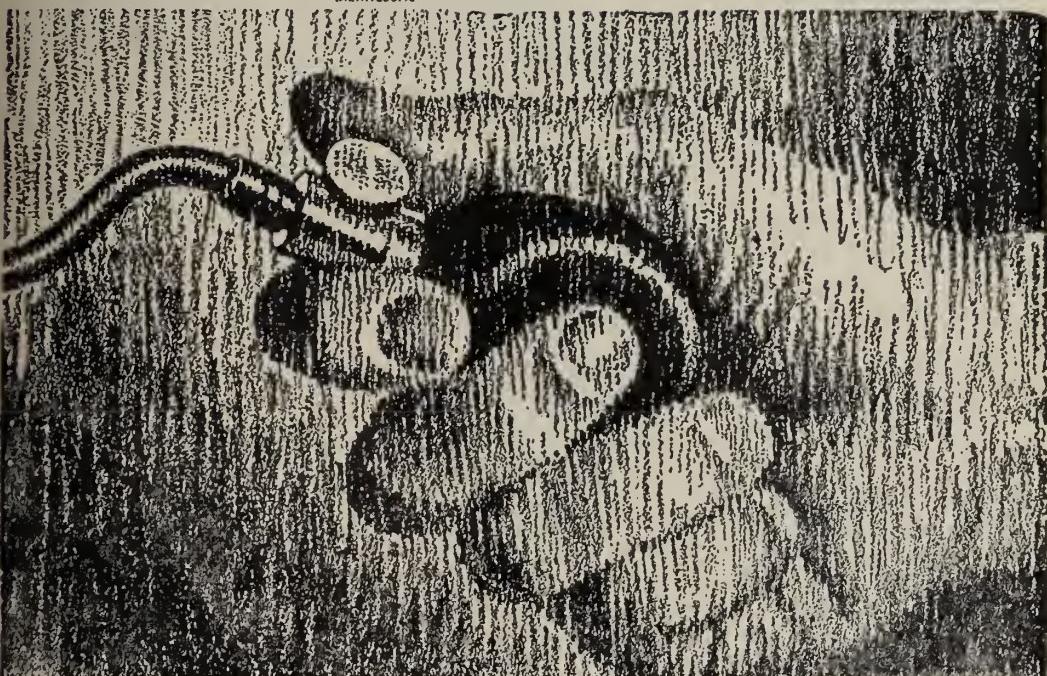
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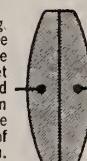
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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



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<sup>1</sup>Practitioner, Nov. 1960, p. 618

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# BOLETIN

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## CARRIER RATE AND ANTIBIOTIC SENSITIVITY OF COAGULASE POSITIVE STAPHYLOCOCCUS AUREUS IN A TROPICAL ENVIRONMENT

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A study of the incidence of *Staphylococcus aureus* coagulase positive in hospitalized patients was carried out in a 200 bed United States Veterans Administration Hospital, at San Juan, Puerto Rico.

The purpose of the study was to determine the nasal carrier rate and antibiotic sensitivity of staphylococci isolated on admission and on discharge of patients; and whether length of hospital stay was related to carrier rate and antibiotic resistance of strains of staphylococci.

### MATERIALS AND METHODS

Nasopharyngeal swabs were taken from 998 patients on admission and cultures repeated on discharge in 550 of these patients.

Specimens were inoculated on trypticase soy blood agar and cultures examined after 24 and 48 hours incubation at 37°C. All staphylococci isolated were tested for coagulase activity. Bacteriophage typing was done on all coagulase positive strains by the method described by Blair and Carr,<sup>1</sup> modified as recommended by the International Sub-committee on Bacteriophage typing of staphylococci.<sup>2</sup> Strains not lysed by the routine test dilution (R.T.D.) were re-examined with a 10-2 dilution of the phage preparation. The pattern of lysis determined the phage type. Twenty two phages, grouped according to the International Committee,

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were employed in this study: Group I — Types 29, 52, 52A, 79, 80; Group II — Types 3A, 3B, 3C, 55, 71; Group III — Types 6, 7, 42E, 47, 53, 54, 73, 75, 77, 83\*\*\*; Group IV — Type 42D; and Miscellaneous Group — Type 81.

Phage preparations and their corresponding propagating strains were originally obtained from Dr. John E. Blair. Phages used in this study were prepared in this laboratory. Discs (BBL) in low and high concentration were used to test susceptibility to penicillin, dihydrostreptomycin, aureomycin, terramycin, tetracycline, chloromycetin, erythromycin, novobiocin and bacitracin. Furadantin was also tested on all strains.

## RESULTS

Table I shows results of cultures from 550 patients studied both on admission and on discharge.

### BOLETIN MEDICO

TABLE I

#### RESULTS OF CULTURES ON ADMISSION AND ON DISCHARGE

GROUPS			Non	Total	Per-
	Typable	Typable	Patients	centage	
Admission Positive-Discharge Positive	79	58	137	25	
Admission Positive-Discharge Negative	27	25	52	9.5	
Admission Negative-Discharge Positive	24	17	41	7.5	
Admission Negative-Discharge Negative	—	—	320	58	
TOTAL PATIENTS STUDIED			550		

One hundred and thirty seven cases (25%) showed positive nasopharyngeal cultures both on admission and on discharge, out of which 79 were typable in both instances, and of these 79 cultures 67 were of the same phage type on both occasions, and 12 were of different phage types on admission and on discharge. Fifty two patients (9.5%) had positive cultures on admission and negative cultures on discharge. Forty one patients (7.5%) showed negative cultures on admission and positive cultures on discharge. Three hundred and twenty (58%) had negative cultures on admission and on discharge.

Table II presents results of cultures for coagulase positive staphylococci on admission and on discharge, after different periods of hospitalization up to seven weeks and over.

\*\*\* Formerly designated as VA<sub>4</sub>.

TABLE II

## RESULTS OF CULTURES ON ADMISSION AND DISCHARGE AFTER DIFFERENT PERIODS OF HOSPITALIZATION

Period of Hospitalization	ADMISSION			DISCHARGE				
	Positive Cultures	Negative Cultures	Total Cultures	Per cent Positive	Positive Cultures	Negative Cultures	Total Cultures	Per cent Positive
1 week	81	135	216	38	78	138	216	36
2 weeks	38	100	138	27	33	105	138	24
3 weeks	34	57	91	37	30	61	91	33
4 weeks	15	30	45	33	14	31	45	31
5 weeks	13	20	33	39	13	20	33	39
6 weeks	1	5	6	17	3	3	6	50
7 weeks	3	7	10	30	3	7	10	30
over 7 weeks	4	7	11	36	4	7	11	36
	189	361	550	34	178	372	550	32

No significant differences were observed between the carrier rate of coagulase positive staphylococci obtained on admission and on discharge of patients during the time periods studied.

Table III shows the results of phage typing and resistance to antibiotics.

No significant differences were observed in the proportion of typable strains, the predominance of Group III organisms, and the phage group distribution of resistant strains obtained on admission as compared with organisms isolated on discharge.

Resistant strains were frequently encountered among phage Group III; 41.5% on admission and 50.4% on discharge. These results are comparable to those obtained by Blair and Carr,<sup>3</sup> and to a previous study done in this hospital.<sup>4</sup>

Table IV shows antibiotic resistant strains of staphylococci: Phage Groups III, III Miscellaneous, and 80/81, cultured on admission and on discharge of patients.

As the total number of typable strains was about the same on admission and on discharge the percentage of resistant strains in both groups is considered reliable. With regard to phages Group III and III — Miscellaneous, the number and percentage was similar on admission and on discharge at the first week of hospitalization. At the second week, the total number of typable strains was cut in half and the percentage of resistant ones increased from forty three on admission to sixty three on discharge. A similar situation was observed on the third and fourth weeks of hospitalization. Thereafter the number of typable strains was too small to warrant any consideration.

By the first week, phage type 80/81 resistant strains increased from thirty three to sixty per cent and from zero to sixty seven per cent by the second week. On the third week, the percentage was the same (100) both on admission and on discharge. Thereafter there were no resistant phage type 80/81 either on admission or on discharge up to periods of over seven weeks when there were no resistant strains on admission but two were cultured on discharge. Again the total number of typable strains,<sup>4</sup> three on admission and three on discharge was very small.

#### COMMENTS AND CONCLUSIONS

The nasal carrier rate of staphylococci among patients on admission and on discharge was not significantly different: 34% and 32%. It is interesting to observe that carrier rates did not increase after periods of hospitalization lasting up to seven weeks. These figures are lower than those for hospital personnel (46% of 323 individuals) as found in a previous study carried out at this

TABLE III  
COMPARISON OF PHAGE GROUPS OF STAPHYLOCOCCI ISOLATED FROM PATIENTS ON  
ADMISSION AND UPON DISCHARGE OF HOSPITAL AND THEIR  
RESISTANCE TO ANTIBIOTICS

PHAGE GROUPS	ADMISSION				DISCHARGE			
	No. of Strains Isolated	Percent	Resistant to one or more antibiotics	Percent	No. of Strains isolated	Percent	Resistant to one or more antibiotics	Percent
Group I	20	10.6	7	35	20	11.2	10	50
Group II	26	13.8	4	15.4	19	10.7	4	21.1
Group III	41	21.7	17	41.5	39	21.8	21	50.4
Group IV	0	0	0	0	0	0	0	0
Miscellaneous	5	2.6	0	0	4	2.2	0	0
I - Misc.	4	2.1	2	50	14	7.8	11	78.6
II - Misc.	3	1.6	2	66.6	3	1.7	1	33.3
III-IV	1	.5	0	0	1	.6	0	0
I - II - III - IV MISC.	1	.5	0	0	1	.6	0	0
Non-Typable	88	46.5	18	20.4	77	43.3	17	22.1
TOTAL STRAINS STUDIED	189	—	50	26.4	178	—	64	35.9

TABLE IV  
ANTIBIOTIC RESISTANT STRAINS OF STAPHYLOCOCCUS AUREUS, COAGULASE POSITIVE  
(PHAGE TYPE GROUP III, III MISCELLANEOUS\*, AND 80/81\*\*) CULTURES ON ADMISSION AND ON DISCHARGE OF PATIENTS

Weeks	ADMISSION						DISCHARGE					
	Total	No. of Group	No. of Resistant	No. of Strains	Total	No. of Typable	No. of Groups	No. of Strains	No. of Resistant Strains	No. of Strains	%	
	No. of Typable Strains	III Misc. and 80/81	%	%	No. of Strains	80/81	III Misc. and 80/81	80/81	80/81	80/81	%	
1 st.	45	18	40	9	50	44	14	32	7	50	60	
2 nd.	22	7	32	3	43	20	8	40	5	63	67	
3 rd.	14	9	64	4	14	16	8	50	5	63	63	
4 th.	10	6	60	1	17	9	7	78	3	43	100	
5 th.	6	2	33	1	50	5	3	60	2	67	0	
6 th.	0	0	0	0	0	0	0	0	0	0	0	
7 th.	1	0	0	0	0	0	1	50	0	0	0	
o,er	2	67	1	50	0	2	0	0	0	0	0	
7	3	0	0	0	3	2	67	2	67	0	0	

\*Groups III and III Misc. on top row.  
\*\*80/81 on lower level

institution.<sup>4</sup> This indicates that a higher nasal carrier rate among employees in daily contact with patients did not necessarily affect the patient staphylococcus carrier rate.

Another interesting observation is the result of cultures on admission and on discharge (Table I). Only 7.5% of patients studied with negative cultures on admission became carriers during hospitalization. About the same number (9.5%) were positive on admission, becoming negative during sojourn in the hospital. This indicates that in this study, hospitalization was not significantly related to variations in the coagulase positive staphylococcus nasal carrier rate.

It is interesting that 25% of individuals had positive cultures on admission and on discharge. Likewise 58% were negative on admission and on discharge.

As to whether length of hospitalization was related to an increased incidence of resistant strains of staphylococci to antibiotics, we feel that evidence available (Table IV) is insufficient to arrive at a definite conclusion. However, a trend in increased resistance appears to have occurred among group III and III Miscellaneous at the 2nd, 3rd, and 4th weeks; likewise in group 80/81, at the 1st, 2nd, and over 7 weeks of hospitalization.

In our institution, patients are housed in spacious wards having no partitions, fifty to sixty individuals in each ward. No air conditioning is used. Cross ventilation is ample. Antibiotic resistant staphylococci phage type 80/81 have been found in hospital personnel, but are only occasionally associated with post-surgical infections and post mortem findings. It is our impression that the conditions stated above are related to the absence of infection outbreaks caused by resistant staphylococci during the past four years. During this period an Infection Control Committee has been in operation at the hospital. The present study indicates that the problem of staphylococcus infection is endemic. No major epidemic outbreak has occurred.

#### SUMMARY

1. Nasopharyngeal swabs were taken from 550 hospital patients on admission and on discharge to determine coagulase positive staphylococcus carrier rates.

2. Nasal carrier rates on admission (32%) and on discharge (34%) after 1-7 weeks hospitalization were not significantly different. These carrier rates among patients are lower than carrier rates among hospital personnel (46% of 323 individuals studied).

3. Length of hospitalization was associated with an apparent increased trend in antibiotic resistant strains of staphylococcus aureus coagulase positive.

## ACKNOWLEDGEMENT

We are grateful to Dr. Américo Pomales-Lebrón, Professor of Bacteriology, School of Medicine, University of Puerto Rico, for his help in carrying out this work and for the preparation of this paper.

## RESUMEN

1. Se obtuvieron hisopos de 550 enfermos hospitalizados, al ingreso y al darse de alta, con el propósito de determinar las tasas de portadores de cepas de estafilococos dorados coagulasa positivos.

2. Las tasas de portadores al ingreso (32%) y al darse de alta (34%) después de una hasta siete semanas de hospitalización no demostraron diferencias importantes. Estas tasas de portadores entre enfermos son más bajas que las tasas de portadores entre empleados del hospital. (46% de 323 personas estudiadas).

3. Aparentemente hubo una tendencia a un aumento en las cepas de estafilococos dorados coagulasa positivos resistentes a los antibióticos asociada a la duración de la hospitalización.

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## INTERRELACIONES ENTRE INFECCION Y NUTRICION\*

NEVIN S. SCRIMSHAW, M.D.\*\*

En esta importante sesión en la que participan distinguidos elementos de la Asociación Médica de Puerto Rico, tendré el honor de tratar un tema de mucha actualidad e importancia, como es el de las

## INTERRELACIONES ENTRE INFECCION Y NUTRICION

### I. INTRODUCCION

En cualquier discusión ecuánime sobre el tema nutrición e infección, se debe considerar no sólo el efecto de las infecciones sobre el estado nutricional, sino también el efecto de la desnutrición sobre la resistencia a las infecciones. El estado nutricional sí influye en la susceptibilidad orgánica a las enfermedades infecciosas y constituye parte muy significativa de la interrelación nutrición-infección. Sin embargo, no siempre se acepta que todas las enfermedades infecciosas tengan algún efecto adverso palpable sobre el balance de nitrógeno y ciertos otros nutrientes esenciales. Estudios llevados a cabo en el Instituto de Nutrición de Centro América y Panamá (INCAP), revelaron que aún la tonsilitis, la otitis media o la presencia de un pequeño absceso estafilocócico disminuían el balance de nitrógeno en niños pequeños.<sup>1</sup> La muy leve infección viral que sigue a la vacunación antivariolosa<sup>2</sup> y a la inmunización con la cepa 17-D de la vacuna contra la fiebre amarilla, también produjeron cambios notables.<sup>3</sup>

El efecto metabólico de una infección, tenga éste significado clínico o de salud pública, depende en gran medida del grado de nutrición adecuada del paciente, al momento en que adquiere la infección. A pesar de ser fácilmente identificable en individuos bien nutridos, es posible que dicho fenómeno carezca de consecuencias prácticas. Sin embargo, en las personas cuyo estado nutricional es ya precario, esto puede llegar a un desenlace fatal. Tales casos son, por supuesto, más comunes en aquellas regiones que no han alcanzado pleno desarrollo técnico.

Las mismas consideraciones se aplican con la misma exacti-

\* Presentado en la Convención Anual de la Asociación Dietética de Puerto Rico celebrada en Río Piedras, Puerto Rico, del 11 al 12 de junio de 1964.

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tud al significado clínico y de salud pública de los estudios experimentales y observaciones en el terreno que demuestran que la resistencia a las infecciones, puede verse afectada por el estado nutricional.<sup>4</sup> Mediante estudios de experimentación y observaciones epidemiológicas, se ha podido establecer en definitiva que un grado severo de deficiencia de casi cualquiera de los nutrientes esenciales, puede alterar marcadamente la respuesta del organismo huésped a la presencia de un agente infeccioso en el medio ambiente. Hay un sinúmero de pruebas que la misma infección puede pasar desapercibida o bien presentarse con caracteres muy leves en una persona bien nutrida, siendo virulenta y hasta fatal en sujetos severamente desnutridos.

Sea que se hable del efecto perjudicial de la infección sobre el estado nutricional, o de la menor resistencia a las infecciones a causa de la desnutrición, la presencia simultánea de ambas —desnutrición e infección— tiene consecuencias mucho más serias para el huésped que cuando una u otra actúan por sí solas.

Este tipo de relación entre la desnutrición y las infecciones puede clasificarse como **sinérgica**. A veces, cuando el agente infeccioso depende en gran medida de los metabolitos de la célula huésped para su supervivencia y reproducción, una deficiencia específica interfiere más con la reproducción del agente que con el funcionamiento normal del huésped. Este fenómeno ha sido comprobado experimentalmente en algunas infecciones virales y en el caso de ciertas infecciones por protozoarios en las que el organismo responsable es primordialmente intracelular.<sup>4</sup> En estas circunstancias la interrelación entre el estado nutricional y las infecciones puede clasificarse de **antagónica**, puesto que la deficiencia nutricional inhibe en vez de favorecer el desarrollo de la infección.

No se tiene conocimiento de ninguna situación en humanos en que el antagonismo haga que la desnutrición resultante de una dieta inadecuada o poco equilibrada, sea de provecho neto para el huésped. Las deficiencias nutricionales de orden natural rara vez adquieren el grado de severidad y de especificidad necesarios para comprobar una acción antagónica, siendo casi siempre sinérgicas con las infecciones bacterianas secundarias que son la complicación y causa de muerte más comunes en las enfermedades de origen viral.

### Consideremos ahora los

#### II. MECANISMOS DE INTERACCION

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### 1. Efecto de las infecciones sobre el estado nutricional

Si bien es cierto que poco se sabe acerca de los efectos metabólicos de las infecciones sobre otros nutrientes, se han establecido definitivamente que el stress de origen infeccioso afecta el balance nitrogenado, incrementando la excreción urinaria de nitrógeno. Cuando hay diarrea severa o la deficiencia es suficientemente grave para afectar la función gastrointestinal, la absorción disminuye también en cierto grado. La menor ingesta dietética debida a anorexia u ocasionada por intolerancia a cantidades normales de alimentos son también factores de importancia. De significado capital en determinadas circunstancias es la tendencia de adoptar durante una enfermedad, dietas terapéuticas ricas en carbohidratos y relativamente deficientes en su contenido proteico y de calorías totales. Esta es una costumbre especialmente nociva en momentos en que el paciente necesita de grandes cantidades de nutrientes esenciales. En el caso de niños preescolares de regiones técnicamente poco desarrolladas, es muy común que tales prácticas formen parte de la cadena de acontecimientos que termina con un episodio fatal de deficiencia proteica severa, esto es, síndrome pluricarencial de la infancia (SPI) ó kwashiorkor.<sup>5</sup>

Cuando se tratan las enfermedades diarreicas en niños, los médicos, así como los propios padres de familia son a menudo culpables de eliminar de la dieta de éstos, los alimentos sólidos y cantidades adecuadas de proteínas. Ya en 1915, Holt padre y su grupo de investigadores habían destacado que la proteína y la grasa no debían sustraerse de la dieta del niño que padecía de diarrea, aún cuando la absorción de estos nutrientes fuese reducida.<sup>6</sup> Dichos autores señalaron que la cantidad absorbida de nitrógeno así como de calorías que vendrían a resultar en un ahorro de proteínas, era directamente proporcional a la cantidad suministrada, y que se obtenían mejores resultados clínicos alimentando a los niños con diarrea, que privándolos de alimento. Chung y Viscorova confirmaron esta conclusión en un estudio que sobre el control de las diarreas llevaron a cabo en Checoslovaquia, y en el que algunos niños fueron tratados con alimentación completa y otros eliminando de su dieta todo alimento sólido.<sup>7</sup> Las experiencias del momento en regiones en proceso de desarrollo técnico sustentan la sabiduría de esta recomendación.

En las regiones tropicales las madres a menudo administran purgantes a sus hijos desnutridos en los que se presenta diarrea, con el fin de eliminar de su organismo los parásitos que erróneamente creen son las que constituyen la causa principal de los sín-

tomas. Esto representa un ejemplo de la asociación que hay entre los factores culturales y las enfermedades infecciosas y que contribuye a empeorar el estado nutricional del niño, en este caso particular —el desarrollo del síndrome de pluricarenza infantil.

Desde hace cierto tiempo se acepta el hecho de que en las personas desnutridas el efecto adverso del stress sobre el balance nitrogenado es menos apreciable que en aquellas bien alimentadas.<sup>8</sup> Este hallazgo ha inducido a algunos investigadores a creer que el balance de nitrógeno levemente negativo, al parecer, en individuos desnutridos que resulta de las infecciones, es menos grave de lo que sería de esperar a juzgar por los resultados experimentales obtenidos en estudios con personas bien nutridas.

Según se ha comprobado en animales de experimentación bien nutridos, así como en humanos, el stress de las infecciones produce un aumento apreciable en la excreción urinaria de nitrógeno, mientras que en un huésped desnutrido, una infección al parecer igualmente severa produce una respuesta mucho menor. Esto sugiere la existencia de cierto mecanismo compensatorio que ayuda al cuerpo a evitar la pérdida de nitrógeno proteico en momentos en que más lo necesita el organismo.

Durante muchos años ha prevalecido el concepto de que la mayor excreción de nitrógeno que se observa durante las infecciones, traumas por accidentes o por intervenciones quirúrgicas, o por abscesos estériles inducidos en animales de experimentación, es esencialmente el resultado del mismo fenómeno, es decir, del daño sufrido por las células. Sin embargo, se ha podido constatar que algunas veces las pérdidas de nitrógeno que, según parece, resultan del stress psicológico, son de la misma magnitud.

Existe poca duda que la destrucción directa de las células ocurra como consecuencia del trauma y, posiblemente también, de algunas infecciones, pero puede ser que en tales casos la destrucción "tóxica" o directamente física, tenga menor significado cuando se trata de explicar la pérdida de nitrógeno, que los efectos endocrinos del stress. Es más probable que las consecuencias de dicho stress, ya sea infeccioso o psicológico y, hasta cierto punto también, de las tensiones traumáticas, sean el resultado final de la actividad suprarrenal aumentada y, consecuentemente, de la mayor secreción de glucocorticoides. Según se sabe, éstas son catabólicas de las infecciones sobre otros nutrientes, se ha establecido disminuye también cierto grado. La menor ingesta dietética al nivel del músculo y anabólicas al nivel de los órganos parenquimatosos.

Aparentemente, en el individuo bien nutrido el nitrógeno se desplaza de los músculos y de otros tejidos en los que es menos esencial, con el resultado de que los niveles de los compuestos ni-

trogenados en el plasma sanguíneo exceden los umbrales del riñón. Por otro lado, en el sujeto mal alimentado los tejidos pueden estar tan depauperados que cualquier exceso de nitrógeno que fluya a la corriente sanguínea como resultado de un estímulo de la corteza suprarrenal, lo asimilan tan rápidamente los tejidos deficientes que la pérdida urinaria es mínima.

De estar este concepto en lo correcto, la magnitud de la respuesta al stress infeccioso —según lo revelan las mediciones por la técnica de balance de nitrógeno— dependería no sólo de la severidad del propio stress, sino también del estado de nutrición del huésped. En otras palabras, el efecto del stress sobre el balance de nitrógeno puede ser importante aún en el caso de que la mayoría del nitrógeno no abandone el organismo, puesto que a la fase catabólica de la reacción al stress, que ocurre al nivel del músculo debe, en última instancia, seguir una fase anabólica en la que el nitrógeno es restaurado a los tejidos de los cuales se desplazó.

No hay ninguna duda de que el nitrógeno de ciertos tejidos es más inestable que el de otros. Cuando la vida del huésped está en peligro, se supone que el nitrógeno que contienen los tejidos menos esenciales se desplaza para el mantenimiento de aquellas funciones más esenciales para la vida. Una vez pasa la crisis, el organismo requiere cantidades extra de proteína a fin de compensar la depleción que ha tenido lugar.

A un individuo bien nutrido no lo afectan períodos cortos de stress que lleguen a agotar sus reservas proteicas, pero en un sujeto malnutrido, ello puede tener graves consecuencias.

Se ha usado el nitrógeno como ejemplo porque es el nutriente que hasta el momento ha sido estudiado más a fondo, pero existen numerosos testimonios de que las mismas consideraciones son aplicables a otros nutrientes esenciales. Ya en 1892, Spicer observó en Inglaterra, que en los niños con meningitis, diarrea infantil, tuberculosis crónica, sarampión, tos ferina y varicela severa, a menudo se presentaba xeroftalmia.<sup>9</sup> Hoy día, en Indonesia, donde las dietas son frecuentemente pobres en vitamina A, se acepta el concepto de que las enfermedades infecciosas, sobre todo el sarampión, son causas precipitantes de xeroftalmia y queratomalacia, enfermedades que tan a menudo causan ceguera.<sup>10</sup>

Se ha demostrado que los niveles sanguíneos de vitamina A se encuentran considerablemente reducidos en niños que padecen de neumonía, artritis reumática, amigdalitis aguda y fiebre reumática.<sup>11,12</sup> En los estudios llevados a cabo en Guatemala sobre el efecto de la vacuna antivariolosa, uno de los resultados más consistentes fue la disminución de los niveles séricos de vitamina A.<sup>13</sup> No obstante que en condiciones normales la vitamina A no es excretada en la orina, esto puede suceder en ciertos estados pato-

lógicos, incluso en casos de neumonía, ictericia obstructiva y nefritis crónica<sup>14</sup>.

Hess, en 1917, hizo notar la frecuencia con que entre los niños de familias de escasos recursos de la ciudad de Nueva York se observaba escorbuto florido después de contraer una enfermedad febril como otitis, neumonía o nefritis.<sup>15</sup> Más tarde se notó este mismo efecto en niños alemanes desnutridos vacunados con la vacuna antivariolosa y, hace poco, los estudios del INCAP han demostrado que durante el momento culminante de una reacción primaria a la vacunación antivariolosa, ocurre un descenso en los niveles sanguíneos de ácido ascórbico y un aumento de esta vitamina en la orina.<sup>2</sup> Si bien es muy poco plausible que en la época actual una infección sea capaz de precipitar escorbuto, ya sea en América del Norte o en Europa Occidental, la facultad que las infecciones tienen de empeorar el estado nutricional es cuando al ácido ascórbico en animales de experimentación, así como en el hombre, aún tiene significado a nivel de la salud pública en muchas partes del mundo.

Por otro lado, se sabe que entre los prisioneros de guerra de los japoneses, cuya alimentación era deficiente en tiamina pero que no presentaban manifestaciones clínicas de deficiencia de esta vitamina, las diarreas infecciosas muy a menudo precipitaban casos severos a y menudo, fatales de beriberi.<sup>19</sup> Se han descrito también casos de esta enfermedad carencial en individuos desnutridos como resultado de un stress adicional, en este caso, pulmonía o paludismo. En regiones del Lejano Oriente todavía privan hoy circunstancias en las que el efecto de las infecciones sobre el estado nutricional en cuanto a tiamina es de importancia capital.

Se sabe que las infecciones crónicas causan la llamada "anemia por infección", casos éstos en que la capacidad de fijación del hierro se encuentra disminuida y el ciclo de vida de los eritrocitos reducido.<sup>17</sup> Según parece, el efecto ocurre por mediación de la corteza suprarrenal y puede simularse en perros, inyectándoles ACTH.<sup>18</sup> En estos experimentos la adrenalectomía abolió la hipoferremia inducida en el animal, aún intacto, por el leve stress resultante de la obtención de muestras sanguíneas o por la administración de ACTH. Más aún, en pacientes con infecciones crónicas, la médula ósea no puede aumentar su producción de glóbulos rojos en el 50% que se requiere para compensar el ciclo abreviado de vida de la célula, mientras que el individuo normal puede incrementar de 6 a 8 veces su producción de eritrocitos. En 28 casos de infección crónica descritos por Clark y sus asociados,<sup>19</sup> en los que un factor concomitante era la reducción de peso, la hemoglobina total disminuyó a un promedio de 59% de los valores calculados a partir del peso normal de los pacientes.

La anemia por deficiencia de hierro asociada a infecciones por anquilostomas prevaleció hace algún tiempo en el sur de los Estados Unidos, y constituye aún un problema de importancia en muchas partes del mundo. La anemia se corrige ya sea mediante una ingesta aumentada de hierro o eliminando los parásitos por tratamiento con antihelmínticos, pero ambas medidas empleadas simultáneamente logran este fin más rápidamente.

Se ha constatado que tanto las infecciones respiratorias espontáneas como los obscesos subcutáneos inducidos con trementina, precipitan la anemia megaloblástica en monos alimentados con dietas deficientes en ácido fólico.<sup>20</sup> Luhby, basado en los resultados de un estudio practicado en 27 pacientes de la ciudad de Nueva York, afectados de anemia megaloblástica, llegó a la conclusión de que las infecciones eran un factor etiológico principal en el desarrollo de este síndrome en cerca de la tercera parte de ellos.<sup>21</sup> Es probable que la anemia por esta causa sea más común en los Estados Unidos de lo que hoy día se supone.

## 2. El efecto del estado nutricional sobre la resistencia a las infecciones

### es otro de los mecanismos de interacción que operan dentro del sinergismo

Según se mencionó antes, hay muchísimas pruebas indicativas de que varios tipos diferentes de deficiencias nutricionales, desde severas hasta moderadas, disminuyen la resistencia a las infecciones. En relación con este punto hay una firme tendencia de dar por sentado que el mecanismo principal de la resistencia a las infecciones es el anamnéstico, es decir, la capacidad orgánica de formar anticuerpos contra organismos específicos o sus toxinas. Indudablemente éste es un factor de resistencia muy importante, y tanto la respuesta primaria como secundaria de formación de anticuerpos a determinado antígeno, puede deteriorarse a causa de deficiencias severas de nutrientes. Esta hipótesis ha sido confirmada en el caso de deficiencias de triptofano, proteína, vitaminas A y D, ácido ascórbico, tiamina, riboflavina, niacina, piridoxina, ácido pantoténico, ácido fólico y vitamina B<sub>12</sub>.<sup>4</sup>

Parte de los primeros trabajos exploratorios en animales de experimentación fueron realizados en conejos por Paul R. Cannon en la Universidad de Chicago hace 20 años o más.<sup>22</sup> Dicho investigador encontró que la deficiencia proteica severa menoscababa la capacidad de producir aglutininas a la fiebre tifoidea y a la paratifioidea. Por otro lado, Whipple y Madden, en Rochester, describieron los mismos resultados en perros depauperados de proteína

que habían estado sujetos a dietas de escaso contenido proteico y a repetidas plasmaférésis.<sup>23</sup>

En Brasil, Budiansky y Da Silva han demostrado que los niños con síndrome pluricarenital de la infancia pierden su habilidad de formación de anticuerpos a la vacuna de la tifoidea,<sup>24</sup> mientras que en México, Olarte y su grupo de investigadores, han obtenido iguales resultados usando la antitoxina de la difteria en niños con ese mismo síndrome.<sup>25</sup> En el curso de un estudio practicado en adultos crónicamente enfermos de Filadelfia, con niveles séricos de albúmina de menos de 4 gramos por 100 mililitros, Wohl y sus asociados encontraron trastornos significativos en la respuesta de anticuerpos de dichos pacientes a la vacuna de la fiebre tifoidea, en contraste con la de individuos cuyos niveles de albúmina sérica excedían esta cifra.<sup>26</sup>

Sin embargo, debe reconocerse que a menudo no hay una correlación directa entre la formación de anticuerpos y la resistencia a la infección.

Se ha encontrado, tanto en animales de experimentación como en pacientes, un alto grado de resistencia a ciertas infecciones, no obstante el no haberse podido demostrar ningún aumento en la titulación de anticuerpos. En contraste se han notificado otros ejemplos en los que se observó muy poca resistencia a las infecciones, a pesar de una marcada respuesta de anticuerpos.

El sistema reticuloendotelial constituye otro medio de defensa en contra de los agentes infecciosos. Cuando se trata de infecciones bacterianas, los leucocitos son, por supuesto, de particular importancia. Basado en estudios clínicos y de experimentación, Doan llegó a la conclusión de que la deficiencia de ácido fólico interfiere con la producción de fagocitos en la médula ósea de los mamíferos, a tal grado que llega a anular el efecto de anticuerpos protectores.<sup>27</sup> Otros investigadores han tenido dificultad en mantener la deficiencia de ácido fólico en monos macacos, debido a frecuente leucopenia, disentería severa y, en última instancia, muerte.<sup>28</sup> Cuando estos animales consumen dietas deficientes, en ellos se desarrolla una notoria gránulocitopenia juntamente con una marcada disminución de resistencia a las infecciones espontáneas.

No es de sorprender que la producción normal de fagocitos se encuentre reducida tanto en animales de experimentación como en el hombre, como resultado de la deficiencia proteica, ya que la depauperación severa de proteínas eventualmente conduce a una marcada atrofia del hígado, bazo y médula ósea, lugares donde se presume que se originan dichos fagocitos.

Guggenheim y Buechler, fundados en los hallazgos de sus trabajos con ratas, llegaron a la conclusión de que las dietas deficientes en proteína "invariablemente" menoscaban la regeneración de

leucocitos, efecto éste que se logra compensar rápidamente mediante la administración de una dieta adecuada en su contenido de proteínas.<sup>29</sup> Ciertamente, los niños con síndrome pluricarencial de la infancia muestran poca o ninguna respuesta leucocitaria a la presencia de infecciones sobreagregadas, y son extremadamente susceptibles a éstas.

La formación de anticuerpos y la actividad leucocitaria entran en juego únicamente cuando el agente infeccioso ha penetrado en el huésped, esto es, una vez ocurre la infección. Hablando reguerosamente, éstos no son mecanismos que evitan la infección, sino que provienen o disminuyen los posibles efectos patológicos de la misma. Un medio de defensa específicamente intrínseco a la prevención de infecciones **per se** es la integridad de la piel de las membranas mucosas y de otros tejidos.

Se sabe que en los tejidos ocurre una diversidad de cambios patológicos, los cuales dependen del tipo y gravedad de las deficiencias nutricionales. Entre éstos cabe citar: a) trastornos de la substancia intercelular; b) disminución o ausencia de secreciones de las membranas mucosas; c) mayor permeabilidad de la pared intestinal y de otras mucosas; d) respuestas fibroblástica disminuida; e) queratinización y metaplasia de las superficies epiteliales; g) pérdida en el epitelio de células ciliadas en el tracto respiratorio; h) edema nutricional con incremento del líquido de los tejidos, i) acumulación de desperdicio celular y moco que proporcionan un medio de cultivo muy favorable. Se desconoce, en gran medida, la importancia práctica relativa de estos cambios. El hecho de que las deficiencias nutricionales interfieren también con la cicatrización de heridas, con la respuesta fibroclástica a traumas locales, con la delimitación de abscesos, y con la formación de colágeno, está estrechamente asociado con su influencia sobre la integridad de los tejidos. Considerada en términos del período total de incapacidad de un individuo debido a infección, la rapidez con que ésta pueda ser localizada y controlada es, a menudo, asunto que amerita consideración especial. Las deficiencias proteicas<sup>30,32</sup> y de ácido escórbico,<sup>33,34</sup> tienen particular propensión a interferir con este proceso de localización.

Desde el punto de vista experimental, la deficiencia de vitamina A ha sido asociada más a menudo con cambios tisulares que favorecen la penetración de los agentes infecciosos. Por ejemplo, un incremento de infecciones respiratorias espontáneas en ratas y perros deficientes en vitamina A se acompaña de metaplasia y queratinización del epitelio del aparato respiratorio.<sup>35,36</sup> Weaver ha demostrado que la mucosa de ciertas partes del tracto gastrointestinal de ratas algodoneras es más vulnerable a los virus de la poliomielitis cuando la dieta es deficiente en vitamina A,<sup>37</sup> y tam-

bien se ha comprobado que la deficiencia de vitamina A, riboflava o tiamina, favorece la penetración de *Salmonella* a la mucosa intestinal.<sup>38</sup>

Además de los tres bien definidos mecanismos de resistencia a la infección: formación de anticuerpos, respuesta leucocitaria e integridad tisular a que me he referido, existe un sinnúmero de otros de significado incierto, cada uno de los cuales posiblemente sea afectado por la desnutrición. Las substancias protectoras no específicas que hay en la sangre, en el fluido peritoneal y en otros fluidos corporales, y que, a menudo, se identifican como lisozimas, se encuentran reducidas, en animales de experimentación sujetos a dietas deficientes. No hay ningún acuerdo definitivo en cuanto a su importancia, no obstante que experimentalmente se ha demostrado que éstas inhiben el desarrollo de virus y bacterias.

La properdina es una euglobulina que se encuentra en el suero normal de todos los animales que hasta el momento han sido sometidos a ensayo y que, según parece, está asociada con la resistencia natural a muchas enfermedades de origen bacteriano o viral y hasta de etiología protozoaria.<sup>39</sup> El interferón es un producto natural que recientemente se ha logrado aislar de células de animales y que aparentemente actúa desligando la oxidación de las reacciones de fosforilación, de modo que la oxidación de la glucosa ya no rinde suficiente trifosfato de adenosina (ATP) para la multiplicación de virus, aun cuando todavía es suficiente para satisfacer las necesidades de la célula.<sup>40</sup> Es de suponer que la formación de cualquiera de estas substancias puede ser afectada por la desnutrición, pero no hay evidencia experimental disponible aún para sustentar tal hipótesis.

No todos los casos de resistencia a las toxinas bacterianas pueden explicarse por la formación de anticuerpos. Las ratas con deficiencias de vitaminas del complejo B o de vitamina A, son más susceptibles a la toxina de la difteria que animales testigo bien alimentados, aun cuando la producción de antitoxinas sea igual y la velocidad de desaparición de la toxina infectante similar.<sup>41</sup> De manera semejante, la reactividad cutánea de cobayos afectados de escorbuto, a la toxina de la difteria aumenta, y el tiempo de supervivencia disminuye.<sup>42</sup> Se ha encontrado, asimismo, que ratas deficientes en vitaminas A y D y en vitaminas del Complejo B, son de 50 a 100 veces más susceptibles a la toxina del tétano que animales testigo.<sup>43</sup> Las dietas, tanto de ayuno breve como las deficientes en proteína, incrementan la susceptibilidad de los ratones a la endotoxina de la *Klebsiella neumonía*, con resultados fatales pocas horas después de haber sido inyectadas y mucho antes de lo que cabría esperar una respuesta de immunización.<sup>44</sup> Este efecto desaparece en el término de 48 horas al administrar a los animales

una buena dieta. Poco se sabe en cuanto a la importancia relativa que en el hombre tiene esta resistencia no específica a las toxinas de origen bacteriano.

Hay, además, una diversidad de ejemplos convincentes de la menor resistencia a las infecciones intestinales que parece estar relacionada con cambios inducidos nutricionalmente en la flora gastrointestinal.<sup>45-49</sup> Más aún, la severidad de las infecciones intestinales causadas por protozoarios y helmintos, a menudo se ve influencia por cambios dietéticos.<sup>50,51</sup> Los trastornos en el peristaltismo gastrointestinal, una secuela de la desnutrición, pueden acentuar también la susceptibilidad a las infecciones entéricas.<sup>52,53</sup>

Es un hecho aceptado que la deficiencia de proteínas y de colina disminuye la función de la glándula suprarrenal, y que la deficiencia de ácido ascórbico está, por lo menos indirectamente, involucrada en la actividad de la corteza suprarrenal. No hay ninguna duda de que la resistencia a las infecciones que presenta un paciente con la enfermedad de Addison o los animales adrenectomizados, se encuentra marcadamente disminuida, pero, ajeno al hecho comprobado de que las hormonas de la corteza suprarrenal pueden tener un efecto inhibitorio directo sobre ciertas endotoxinas bacterianas,<sup>54</sup> no se conoce a ciencia cierta el mecanismo de la acción corticoide en el caso de infecciones. De manera semejante, se tiene más conocimiento que comprensión sobre la susceptibilidad de los diabéticos a las infecciones, sobre todo a aquellas de naturaleza localizada.

De los conceptos vertidos se deduce claramente que son varios y diversos los mecanismos implicados en la resistencia a las infecciones y que éstos son influenciados por la desnutrición de muy diferentes maneras. El grado hasta dónde uno u otro de estos mecanismos sea de capital importancia para explicar el sinergismo depende del agente infeccioso, de las deficiencias de nutrientes y del estado del huésped. Esto es, sencillamente, otro modo de decir que los factores que integran la terna epidemiológica clásica: huésped, agente y medio ambiente, están todos implicados tanto en la producción de enfermedades infecciosas, como nutricionales. Según la predominancia de los signos clínicos, la infección y la desnutrición cambian de lugar, ocupando los sitios de agente o medio ambiente, respectivamente.

**Me referiré ahora al**

## **B. Antagonismo**

**puesto que**

Una discusión de los mecanismos de interacción no sería com-

pleta sin antes mencionar en mayor detalle la naturaleza del antagonismo entre la desnutrición y los agentes infecciosos. No es difícil explicar el hecho de que en la vía experimental, las deficiencias severas específicas de nutrientes individuales —especialmente cuando éstas son acentuadas por el uso de antagonistas metabólicos al nutriente en cuestión— disminuyen la gravedad de algunas infecciones virales y protozoarias intracelulares y agudizan en el huésped las consecuencias de la invasión por rickettsias, bacterias o helmintos. El antagonismo ocurre con mayor frecuencia cuando los organismos ya no pueden obtener los metabolitos específicos que necesitan, porque la deficiencia responsable ha alterado el metabolismo de las células del huésped.

### Examinemos ahora la

#### III. LA IMPORTANCIA PRACTICA DE LA RELACION ENTRE LA NUTRICION Y LAS INFECCIONES

Considerado desde un punto de vista global, el sinergismo entre nutrición e infección es en gran medida el factor responsable de la alta mortalidad resultante de las infecciones en regiones técnicamente poco desarrolladas. Por ejemplo, el sarampión es una enfermedad casi universal en todos los conglomerados de poblaciones. En los Estados Unidos de América y en Europa muchos niños murieron a causa de ella hace 50 años o más. Hoy día el sarampión rara vez es fatal en dichas áreas, hecho que principió a observarse antes del advenimiento de las sulfonamidas y antibióticos que en la actualidad pueden controlar las complicaciones bacterianas de ésta y de otras enfermedades de origen viral; lo que es más, dichas complicaciones se presentan muy de vez en cuando en un niño bien nutrido.

En las cercanías de la ciudad de México, sin embargo, la tasa de mortalidad por sarampión, por 100,000 habitantes en 1956 fue 164 veces más alta que en Estados Unidos, y en la República de Guatemala, 228 veces mayor.<sup>55</sup> No es la virulencia del virus en sí el factor que difiere en estos casos, sino más bien la poca resistencia que a la enfermedad presenta el niño desnutrido. Esto puede confirmarse comparando la gravedad del sarampión en familias de alto y bajo nivel socioeconómico en regiones en vías de desarrollo.

En Guatemala el INCAP lleva a cabo un programa de alimentación suplementaria por cuyo medio suministra, dos veces diarias, leche e Incaparina, una mezcla vegetal de bajo costo y alto contenido proteíco, a todos los niños menores de cinco años de edad de una comunidad indígena rural. En un segundo pueblo, seme-

jante al primero, únicamente proporciona tratamiento médico y además se han mejorado las condiciones sanitarias de la localidad, pero no desarrolla ninguna actividad de carácter nutricional. Una tercera comunidad, cercana a las dos primeras, forma parte de dicho estudio y sirve como testigo. El año pasado una epidemia de sarampión atacó a las tres poblaciones con el resultado de un total de 40 a 60 casos entre los niños de edad preescolar. En el pueblo testigo murieron 5 de ellos y en el llamado "de tratamiento", la tasa de mortalidad fue similar. En la comunidad donde los niños reciben el suplemento dietético solamente se registró una defunción y este caso fue un niño cuyos padres no le permitieron participar en el programa. También se ha observado que los episodios de diarrea infecciosa en los niños que reciben alimentación complementaria son menos frecuentes y menos severas.

El mayor número de observaciones del efecto del estado nutricional sobre la resistencia a las infecciones han sido realizadas con enfermos de tuberculosis. Antes de que se pudieran utilizar las técnicas quimioterapéuticas de reciente aplicación, la tuberculosis era a menudo una enfermedad fulminante y con frecuencia, fatal. Las personas bien nutridas, por supuesto, también eran susceptibles de infección, pero en ellas la enfermedad no cobraba caracteres tan severos.

Dos investigadores, Orr y Gilkes, encontraron que la tuberculosis, la artritis reumática y las infecciones respiratorias fatales eran mucho más comunes en una tribu africana que consumía una dieta en la que predominaban los cereales, que en otra que ingería considerables cantidades de leche y huevos. Lo que es mas, el agregado de leche, carne y vegetales verdes a las dietas de los sujetos consumidores de cereales indujo un descenso en la prevalencia y severidad de tales infecciones.<sup>56</sup>

La causa principal de muerte en el síndrome pluricarencial de la infancia, es la infección superpuesta, pero una vez el niño principia a responder al tratamiento dietético, ya no hay por qué temer a esta complicación. Debido a que la respuesta a las infecciones, tanto febris como leucocíticas, no parece figurar en el SPI, la presencia de infecciones intercurrentes en este síndrome pasa generalmente desapercibida hasta tanto se toma una radiografía del tórax o bien se practica la autopsia.

En la época en que el escorbuto clínico todavía era frecuente en los Estados Unidos, los niños que padecían de esta deficiencia tenían una mayor incidencia de infecciones como adenitis, otitis y nefritis<sup>57</sup>. La pelagra ha sido asociada con una mayor presencia de infecciones estafilocócicas y estreptocócicas, así como con la estomatitis producida por la espiroqueta de Vincent<sup>58</sup>. Hace apenas algunos años, en 1955, Jelliffe dio cuenta de un 30% de mortalidad

entre niños africanos desnutridos con estomatitis úlceromembranosa que representaban gingivitis supurativa<sup>59</sup>. Se ha informado, asimismo, que la hepatitis es más severa entre las tribus africanas desnutridas<sup>60</sup>.

Durante la Segunda Guerra Mundial era experiencia común en los campos de concentración del Lejano Oriente encontrar amebiasis severa asociada con períodos de privación dietética aguda<sup>61</sup>. Elsdon-Dew, por ejemplo, encontró que la disentería amebiana fulminante aguda era más común entre los Bantú, tribu africana cuya dieta es a base de maíz, que entre los hindúes consumidores de arroz con "curry" y entre los europeos de África del Sur alimentados con dietas bien equilibradas<sup>62</sup>. Se ha informado también que la mortalidad por paludismo es significativamente mayor entre los pacientes desnutridos<sup>63</sup>.

En muchas regiones del mundo la relación sinérgica entre la desnutrición y la mayoría de las infecciones forma aún parte destacada de los problemas globales de salud. Hasta tanto se observe que de una cuarta parte a la mitad de todos los niños nacidos vivos en un país mueren antes de cumplir los 5 años, el sinergismo entre la desnutrición y las infecciones seguirá siendo un factor de importancia<sup>64</sup>. La nutrición debe ocupar alta prioridad en los programas de salud que se desarrollan en la mayor parte de los países menos desarrollados. La situación real no la revelan las estadísticas vitales a nuestro alcance. Por ejemplo, cuando se acordó investigar las causas de muerte entre los niños pequeños de cuatro comunidades rurales de Guatemala acaecidas en 1956 y 1957, sólo una del total de 222 defunciones notificadas figuraba en los registros oficiales como debida a desnutrición<sup>65</sup>. Este fue un caso de la serie investigada que murió en un hospital y el único en que la causa de muerte había sido certificada por un médico. Los estudios de campo revelaron que algo más de la tercera parte de las muertes podían considerarse debidas a desnutrición, una tercera parte a diversos tipos de infecciones gastrointestinales y la última parte a infecciones respiratorias. La mayoría de las defunciones por desnutrición eran casos de síndrome pluricarenencial de la infancia precipitados por una infección. La mayor parte de esas muertes por infección no habrían ocurrido de haber afectado ésta a niños bien nutridos.

Desgraciadamente, se presta tan poca atención a la nutrición en muchas escuelas de medicina y salud pública que los médicos y las personas que trabajan en el campo de la salud pública a menudo se olvidan de que la nutrición es parte importante de sus propias actividades y programas. Es por ello que el médico que recibe adiestramiento en Estados Unidos o el trabajador en salud pública de países técnicamente poco desarrollados, sea o no nacional,

tiende a prestar poca consideración a la nutrición, aun cuando ésta es un problema de capital importancia.

#### RESUMEN

La gran variedad de pruebas derivadas de estudios clínicos, de laboratorio y de campo, sugieren que la interacción entre las infecciones y la desnutrición, en el hombre, es importante, tanto desde el punto de vista clínico como desde el ángulo de la salud pública. Esto es particularmente apreciable entre las personas de grupos socioeconómicos inferiores en países menos desarrollados. En aquellos casos en que existe ya un estado de desnutrición clínica o subyacente, las enfermedades infecciosas a menudo precipitan la desnutrición severa, y las infecciones pueden tener consecuencias más graves de lo que cabría esperar si se tratase de un huésped bien nutrido.

Se ha demostrado que la desnutrición interfiere con la formación de anticuerpos, actividad fagocítica, integridad y reparación de los tejidos, mecanismos de resistencia no específicos, y todos aquellos factores que afectan la resistencia a las infecciones, tales como la flora intestinal y el balance endocrino. Las deficiencias nutricionales de proteína, y de las vitaminas A y C son especialmente propensas a disminuir la resistencia a las enfermedades infecciosas.

En vista de que en las regiones menos desarrolladas la desnutrición prevalece sobre todo entre los niños preescolares, el problema del sinergismo entre la desnutrición y las infecciones es también más grave en este grupo de edad, y da cuenta de las altas tasas de mortalidad que se observan entre los niños de 1 a 4 años de edad en dichas zonas.

Cuando tanto la desnutrición como el hecho de estar expuestos a las infecciones constituyen problemas graves, como es el caso en la mayoría de regiones tropicales y países menos desarrollados, el éxito que se tenga en el control de la desnutrición o de las enfermedades infecciosas, dependerá de los esfuerzos que se haga para combatir ambas condiciones.

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## ELECTRICAL CONVERSION OF ATRIAL FIBRILLATION WITH A DIRECT CURRENT SHOCK

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### CASE REPORT

#### Historical background

Almost 200 years ago in 1774 John Aldini,<sup>1</sup> a nephew of Galvani, reported to the Royal Humane Society the resuscitation of a three year old child with the use of electric shocks through the chest. Aldini himself was the first to apply an electrode directly to the heart of a criminal two hours dead. He was unable to produce a contraction of the heart. At about the same time, Vassalle from Turin obtained heart contractions by direct stimulation of the heart of decapitated prisoners. In 1899 Prevost and Batelli introduced alternating current countershock; they first employed direct current to fibrillate and to defibrillate the heart. Thirty years elapsed before the subject of electrical defibrillation was re-investigated.

Kowvenhaven, Hooker and Langworthy in experiments conducted in the early 1930's, established the foundation for the present use of electrical countershock. In 1947 Beck successfully defibrillated a human heart with complete recovery of the patient.

Almost 150 years after Aldini and Vassalle, Zoll successfully employed external electrode stimulation to arouse the heart in a patient with ventricular standstill secondary to a complete heart block. Five year later in 1957 Lillehei and Allen successfully applied direct myocardial stimulation to patients with operatively induced heart block.

During the past three years Lown<sup>2,3</sup> has introduced and popularized the use of direct current (D.C.) shocks in cases of ventricular fibrillation and in many other types of cardiac arrhythmias. It is important to note that the treatment of cardiac arrhythmias with the use of drugs, has changed very little in the 45 years since Frey introduced the use of quinidine.

### CASE REPORT

This 33 years old male was admitted to the University of Puerto Rico Hospital with a diagnosis of mitral insufficiency. He had rheumatic fever in early childhood with progressive limitation of physical activities.

On admission the pulse was irregular with an apical rate of 80 per minute. The BP was 130 '80. On physical examination he

had cardiomegaly and a grade III systolic murmur at the apex irradiating to the axilla.

The patient underwent replacement of his mitral valve with size No. 4 Starr Edwards ball-valve prosthesis on April 10, 1964. The early post operative course was uneventful except for persistent atrial fibrillation, the ventricular rate being 60 per minute. At that time the patient was on a 500 mg. salt diet and receiving 0.1 mg. of digitoxin daily. Six days following operation 200 milligrams of quinidine sulfate by mouth was administered every 6 hours and electrical conversion was scheduled 2 days thereafter. The last dose of quinide was given intra muscularly. Under very light sodium pentothal anesthesia and oxygen by mask a 100 watt sec.\* electrical shock was administered. As can be seen from Figure 1, he converted immediately to a normal sinus rythm. A few minutes after the electric shock the patient was fully awake. Quinidine was maintained for three weks after the electric conversion and at present he is still taking digitoxin and has maintained his normal sinus rythm.

#### Discussion:

It is important to realize that successful conversion depends primarily upon correction of the underlying pathologic lesion. If such is achieved D.C. electric conversion is a safe and simple means of improving the cardiac status of these patients. The advantages of direct current over alternating current defibrillation are well established<sup>6,7</sup> and its discussion is not within the scope of this report. Electric shock defibrillation is of course not limited to post operative arrhythmias but can be utilized in many situations where conversion is otherwise resistant to drug therapy.

#### Summary and Conclusions:

The successful conversion of a patient's rythm from persistent atrial fibrillation to normal sinus rythm following mitral valve replacement is reported.

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\* Utilizing The American Optical Lown Cardioverter.

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## **COMBINED ANTIDEPRESSANT-TRANQUILIZER REGIMEN IN DEPRESSED PSYCHOTICS**

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Many patients who are successfully treated with the newer antidepressant drugs simply trade their depression for anxiety or other emotional turmoil that had not been evident before in their symptomatology. Whether antidepressants actually provoke such a state directly by drug action or indirectly by effectively lifting depression is difficult to say. Either way, it makes little difference to the patients or their physicians. In an effort to reduce the anxiety seen in these cases, we began a trial combination of an antidepressant drug and a tranquilizer drug empirically, in hospitalized patients with acute and chronic depressive psychoses and with depressive symptomatology. This paper reports the results of a trial in which tranylcypromine (Parnate) and trifluoperazine (Stelazine) were the drugs used. Both drugs are generally available in most countries and have been extensively studied in the Americas and abroad.<sup>1-8</sup>

### **Technique and Procedure**

Thirty patients were selected: the fifteen women in the series were between the ages of 31 and 71 years (average age: 48.5 years); the fifteen men were between the ages of 18 and 60 years (average age: 32.2 years). Six of the women were first admissions and 9 were readmissions; four had previously been treated in the Outpatient Clinic without improvement. Five of the men were first admissions, while 10 were readmissions; seven of them had been treated in the Outpatient Clinic without improvement.

Before and at the end of nine weeks of treatment, each patient received a complete physical and neurological examination and underwent a battery of laboratory tests. Physical findings before treatment were essentially negative in all but five patients. Of these five, two had acute bilateral otitis externa — one responded promptly to antibiotic treatment and one did not; one had severe iron deficiency anemia due to malnutrition and parasitosis and was given adjunctive iron therapy parenterally; one had moderate high blood pressure which disappeared two days after treat-

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ment with tranylcypromine and trifluoperazine was started; and one had advanced, active tuberculosis of the lungs and continued to receive the specific therapy she had been receiving for more than a year.

The laboratory tests conducted on these patients included: complete blood counts, blood sugar, urea nitrogen, serum transaminases (both SGOT and SGPT), Hanger's test, and serum alkaline phosphatase. In 27 of the 30 patients Hanger's test showed evidence of abnormalities (3+ or 4+ in 48 hours) before treatment. Otherwise, all other tests were within normal limits at the start of the study, except for the one patient with anemia. Pulse and blood pressure were checked frequently and body weight was recorded weekly.

The diagnosis present in the study group are listed below:

#### Women

- 4—Manic-depressive reaction  
in the depressive phase
- 4—Depressive psychosis
- 4—Involutional psychosis
- 2—Paranoid schizophrenia
- 1—Schizo-affective schizophrenia

#### Men

- 7—Depressive psychosis
- 2—Involutional psychosis
- 2—Paranoid schizophrenia
- 1—Undifferentiated chronic schizophrenia
- 1—Undifferentiated acute schizophrenia
- 1—A.B.S. due to alcoholism and psychosis
- 1—Manic-depressive reaction in the depressive phase

Assessments were made by raters who used a guide list of characteristic symptoms (see Table 1) and noted whether or not the symptoms were present.

We began treatment with the following regimen:

First week: 10 mg. tranylcypromine twice a day; and 1 mg. trifluoperazine twice a day;

Second week: 10 mg. tranylcypromine three times a day; and 2 mg. trifluoperazine twice a day;

Third week: 10 mg. tranylcypromine three times a day; and 4 mg. trifluoperazine twice a day (tranylcypromine was not increased during this week);

Fourth week: 10 mg. tranylcypromine and 5 mg. trifluoperazine twice a day.

All the men began to improve by the fourth week, except one

TABLE 1  
DEPRESSIVE SYMPTOMS

Insomnia	Pessimism
Disturbed sleep	Crying without reason
Absurd dreams	Affective lability
Early awakening	Guilt feelings
Decreased appetite	Feelings of despondency
Bad taste and dryness of the mouth	Feelings of indignity or lowliness
Polydipsia	Feelings of unreality
Constipation	Fear of insanity
Nausea	Fear of physical illness
Thoracic pressure	Fear of death
Palpitations	Attacks of anxiety
Coldness of the extremities	Suicidal thoughts and tendencies
Cephalalgia	Psychomotor retardation
Cerebral throbbing or hammering	Poor concentration and memory
Heaviness in head and neck	Will - indecision
Pain in the shoulders	Apathy - loss of interest in things
Cramps	Morbid desires for death, self-destruction
Warmness	Pseudoperceptions, illusions
General feeling of coldness	Hallucinations
Asthenia	Delirious ideas
Dizziness	Hypochondria
Blurred vision	Religious
Hypolibido or hyperlibido	Sin and guilt
Metrorrhagia	Indignity or lowliness
Gray mood	Persecution
Sad mood	Jealousy
Anxious mood	Matrimonial and family conflicts
Irritable mood	Personality changes
Sociopathic conduct (alcoholism, play)	Negligent about personal cleanliness

who, besides taking drugs, was given a course of 3 ECTs weekly for two weeks. For the men, therefore, the dosage levels reached by the fourth week were maintained for the remaining five weeks of the study. For the women, response was less consistent and required some adjustment of dosage. For instance, when side effects occurred and persisted for several days, trifluoperazine (but not tranylcypromine) dosage was reduced. Or when no improvement occurred by the end of the fourth week of treatment and the women appeared to be tolerating the drugs, dosage was increased at the rate of 10 mg. of tranylcypromine and 2 mg. of trifluoperazine weekly for the next two weeks. The highest dosages used in this series were 60 mg. of tranylcypromine and 15 mg. of trifluoperazine. (When the trifluoperazine dosage reached 14 mg., it was more convenient to dispense three 5 mg. tablets instead of both 2 mg. and 5 mg. tablets used during the fifth and sixth weeks.) The dosage in women who had improved or who

had begun to improve by the fourth week was not increased further.

## Results

In the pretreatment psychiatric assessment, the women displayed a total of 464 depressive symptoms, that is, approximately 30 depressive symptoms per patient. By the ninth week of treatment these symptoms had decreased to 234, with the final average being about 15 per patient. Improvement, when it occurred, generally began in the second week and became more apparent during the third week. Two patients (No. 8 and 15), however, took longer to respond, showing improvement in the eighth and fourth weeks, respectively. In two other patients (No. 11 and 13) great improvement was noted between the fourth and seventh weeks, but it proved transient, with the patients becoming worse by the eighth week and ending treatment without improvement. In all, six patients were discharged as cured; six showed no improvement; and 3 improved slightly. (See Table 2) Average weight change ( $-0.03$  lbs.) during treatment was not significant.

In the pretreatment psychiatric assessment, the men displayed a total of 396 depressive symptoms, that is, an average of about 26 symptoms per man. By the ninth week of treatment, these symptoms decreased markedly to a total level of 21, approximately to a level of 1 to 2 symptoms per man. Fourteen patients were discharged as cured during this time: 12 with total remission of symptoms and 2 with partial remission. In one patient (No. 12), although his depressive symptoms subsided, the psychosis remained unchanged. (See Table 3) The 15 men gained a total of 116 lbs. for an average weight gain of approximately  $7\frac{1}{2}$  lbs.

All but one of the men began to improve by the third week of treatment; Patients 2, 10, and 13 were discharged as cured during the fourth week, and thereafter were seen weekly at the Out-patient Clinic. Patient 3 did not respond to drug therapy until, as mentioned before, he also received 6 ECTs (3 a week) during the fourth and fifth weeks.

As for side effects, two men (No. 4 and 14) reported diarrhea, which disappeared without countermeasures or suspending therapy; we therefore believe that their diarrhea was not related to the drugs. Side effects in the women occurred more often and seemed drug related: 4 reported dizziness; 2, trembling; 2, abdominal pain; and 2, vomiting. In 4 women, however, the side effects disappeared spontaneously; in the other four, they subsided when the dose of trifluoperazine was lowered.

TABLE 2. CLINICAL CHARACTERISTICS AND RESPONSE TO COMBINED  
ANTIDEPRESSANT-TRANQUILIZER REGIMEN IN HOSPITALIZED  
WOMEN PSYCHIATRIC PATIENTS

WOMEN	Weekly Psychiatric Assessment						Assessment of Depressive Symptoms			I.W.*	F.W.*
	WEEKS	1	2	3	4	5	6	7	8		
(1) G. de L. D., white, 48 years old, 3rd attack, 000-796**	19	15	10	4	1	1	1	1	1	105	115.5
(2) A. F. G., white, 70 years old, III for 20 years, 000-X24	28	27	23	21	18	17	17	15	16	156	160
(3) M. F. C., negro, 69 years old, II for one year, 000-X14	27	27	27	26	27	27	26	30	28	129	128
(4) R. G. I., white, 37 years old, 2nd attack 3/62, 000-X12	44	36	21	10	4	1	1	1	1	153	159.5
(5) L. G. H., negro, 31 years old, ill for 2 years, 000-X14	38	35	32	14	0	0	0	0	0	106	116
(6) C. I. L. T., negro, 36 years old, 1st attack 4/62, 000-X12	40	36	23	22	3	0	0	0	0	160	168
(7) M. M. R., negro, 46 years old, ill for 3 years, 000-796	16	14	20	24	25	24	20	16	14	119	94.5
(8) A. Q. de W., negro, 46 years, 4th attack, ill for one year, 000-X13	32	34	30	35	34	32	34	30	24	174	176
(9) I. P. P., white, 49 years old, ill for 3 years, 000-796	39	19	4	2	1	1	1	1	1	129	133
(10) I. R. G., white, 71 years old, ill for 30 years and hospitalized for 6 years, 000-X24	37	39	39	41	40	18	39	37	39	146	132
(11) M. F. A., white, 33 years old, 1st attack 15 years ago, 000-X27	24	22	17	2	3	7	17	19	20	172	167
(12) P. S. L., white, 33 years old, ill for 3 years, 000-X14	31	31	33	35	28	30	31	29	28	115	120
(13) J. T. de E., white, 62 years old, various attacks, last one more than a year ago, 000-X13	38	37	28	24	20	24	27	30	34	130	124
(14) C. P. M., mulatto, 48 years old, 2nd attack, ill for 20 days, 000-796	25	25	22	21	22	25	22	24	24	92	94
(15) M. I. V. M., white, 48 years old, 1st attack 2/62, 000-X14	26	28	25	7	1	1	0	0	0	92	94
	464	425	357	289	226	225	239	231	230	1,978	1,977.5

\* I.W.: Initial Weight      \*\* F.W.: Final Weight  
\*\* American Psychiatric Classification

TABLE 3. CLINICAL CHARACTERISTICS AND RESPONSE TO COMBINED  
ANTIDEPRESSANT-TRANQUILIZER REGIMEN IN HOSPITALIZED MEN  
PSYCHIATRIC PATIENTS

MEN	Weekly Psychiatric Assessment of Depressive Symptoms							I.W.*	F.W.*
	WEEKS	1	2	3	4	5	6		
( 2 ) L. C. de J., white, 60 years old, 1st attack, 1st attack, admission 1/62, 000-X24**	25	27	4	0	0	0	0	0	112
( 2 ) L. C. de J., white, 60 years old, 1st attack, admission 3/62 (7 months' duration), 000-796	16	11	6	0	0	1	8	0	129
( 3 ) C. G. C., white, 39 years old, 2nd attack 3/62 (6 E.C.T. in 2 weeks), 000-X14	16	16	16	3	3	2	0	0	106
( 4 ) A. L. N., white, 19 years old, 1st attack 3/62, 000-X14	25	28	19	13	1	0	0	0	101
( 5 ) J. O. S., white, 28 years old, 1st attack 3/62 (two months' duration), 000-X25	37	38	19	13	6	5	5	5	119
( 6 ) P. M. G., white, 28 years old, 1st attack 3/62, 1½ years of treatment in Outpatient Clinic, 000-X14	23	23	23	11	11	10	10	10	136
( 7 ) J. M. T., white, 38 years old, third attack 2/62 (17 E.C.T. previously), 000-X14	29	29	25	20	3	3	2	2	142
( 8 ) L. O. M., white, 25 years old, 2nd attack 4/62, 000-X14	35	35	16	0	0	0	0	0	143
( 9 ) C. B. R., white, 45 years old, 2nd attack 3/60, 000-796	31	31	29	8	8	5	0	0	132
(10) R. P. T., white, 18 years old, 1st attack 3/62 (4 months' duration), 000-3312 and psychosis	16	16	5	0	0	0	0	0	125
(11) R. A. M. T., white, 30 years old, 3rd attack 3/62 (15 days' duration), 000-X14	21	21	9	2	0	1	0	0	120
(12) B. C. V., negro, 33 years old, 4th attack 9/61, 000-X26	29	27	20	7	4	4	4	4	143
(13) J. V. N. M., white, 33 years old, 2nd attack 4/62 (5 months' duration), 000-X14	35	32	31	2	2	0	0	0	103
(14) A. L. R. C., white, 37 years old, 2nd attack 4/62 (2 months' duration), 000-X24	33	23	15	3	2	1	0	0	147
(15) M. R. M., white, 45 years old, 2nd attack 3/62, 000-X12	24	22	14	4	0	0	0	0	142
	396	379	251	83	37	33	29	21	1,940
									2,075

\*\* American Psychiatric Classification

\* I.W.: Initial Weight

\* F.W.: Final Weight

## SUMMARY

Of the 30 patients with depressive symptomatology (15 men; 15 women), 20 were discharged as cured during the course of nine weeks' treatment with tranylcypromine and trifluoperazine in combination; 18 exhibited total remission of symptoms, 2 had partial remission of symptoms. The 10 remaining patients showed little or no improvement. The best results in women were obtained in those with manic-depressive reaction, involutional psychosis, and depressive psychosis, in that order; the worst results were obtained in schizophrenia with depressive components. In men excellent results were obtained regardless of diagnosis, although one of the 15 required a short course of EST.

The effective daily dosage of this combination seems to be 40 mg. tranylcypromine and 10 mg. trifluoperazine, given in divided doses and arrived at gradually by increasing dosage of the two drugs over a course of 4 weeks. In unresponsive patients, increasing the dosage beyond these levels did not produce favorable results. Drug related side effects — dizziness and trembling — seemed due mainly to trifluoperazine. From the findings of the present investigation, coupled with past clinical experience, the combination of tranylcypromine and trifluoperazine is a valuable therapeutic means to treat psychotics with prominent elements of depression in their symptomatology.

## RESUMEN

Treinta enfermos hospitalizados, 15 hombres y 15 mujeres, con psicosis depresiva aguda y crónica y con sintomatología depresiva, fueron tratados con una combinación de tranilcipromina ('Parnate') y trifluoperazina ('Stelazine'). De los 30 enfermos, 20 fueron dados de alta por curación durante el curso de nueve semanas de tratamiento —18 experimentaron una remisión total de los síntomas y dos parcial. Las 10 pacientes restantes accusaron poca o ninguna mejoría. Los mejores resultados en las mujeres se obtuvieron en las que sufrían de reacción maníaco-depresiva, psicosis involutiva y psicosis depresiva, en el orden citado; los peores resultados fueron obtenidos en las esquizofrénicas con manifestaciones depresivas. En todos los casos del sexo masculino se obtuvieron resultados excelentes, aún cuando uno de los 15 hubo de someterse a un corto tratamiento electroconvulsivante.

La dosis eficaz de esta asociación medicamentosa parece ser de 40 mg. de tranilcipromina y 10 mg. de trifluoperazina, administrada en dosis fraccionadas, llegándose a dicha dosis de modo gradual por incrementos de los dos medicamentos durante el curso de

4 semanas. En aquellos pacientes que no se obtuvieron resultados favorables, el aumento de los dos medicamentos mencionados hasta llegar a una dosis diaria superior a la señalada, no mejoró los resultados obtenidos. Efectos secundarios producidos por el medicamento —vértigo y temblor— parecen ser producidos principalmente por la trifluoperazina. De los resultados de la presente investigación, junto con la experiencia clínica obtenida anteriormente, la asociación de traniccipromina y trifluoperazina es un procedimiento terapéutico útil para tratar a los psicóticos con manifestaciones destacadas de depresión en su sintomatología.

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## **ARTICLE OF MEDICAL INFORMATION:**

### **WHEN YOUR PATIENT FILES FOR DISABILITY BENEFITS...**

*F. A. RODRIGUEZ FORTEZA, M.D.*

Almost every practicing physician in Puerto Rico is asked by his patients from time to time to furnish medical evidence in support of their claims for social security disability benefits. Last year about 10,000 medical reports were submitted on behalf of Puerto Rico applicants. During the next 12 months 6,500 Puerto Rico residents are expected to file disability claims. Judging from past experience, about one-half of these people will be found to have medical conditions severe enough to qualify as "disabled." They will join the more than 5,500 disabled Puerto Ricans and 10,000 of their dependents who are currently drawing social security disability benefits at a rate of \$480,000 a months.

#### **How A Patient May Qualify For Benefits**

To qualify for social security disability benefits, the patient must have a physical or mental impairment which prevents him from doing any substantial gainful activity. This is not an occupational definition. A person who is prevented by an impairment from doing his accustomed or prior work, but who has the capacity for other substantial work, considering his educational and vocational background, will no be found disabled under the law.

The injury or illness must be medically determinable—that is, demonstrable through the diagnostic techniques of medicine. It must have prevented work for 6 months and must be expected to be of long-continued and indefinite duration despite therapy. Benefits do not begin until after this 6-month waiting period.

In addition to meeting the medical requirements, a worker must be insured, i.e., he must have worked under social security for at least 5 years out of the 10 years before becoming disabled.

#### **Applying For Disability Benefits**

Puerto Rico residents may apply for disability benefits at any of the five social security district offices throughout the Commonwealth. The district office gives the applicant information about his rights, helps him to fill out his application, and advises him as to the proofs and documents he may to support his application. Through a comprehensive interview designed to help the applicant recall and describe the facts that may have a bearing on

his claim, the district office records the applicant's major complaints, his daily activities, his educational and vocational background, how his impairment interferes with his ability to work, and other significant facts.

Each applicant is required to furnish, at his own expense, medical evidence in support of his claim and a medical report form is sent to be completed by his attending physician and other sources of treatment. The medical evidence in support of disability claims is thus drawn largely from sources in the claimant's own community, usually as a by-product of the medical care he is receiving. The reporting physician may use the medical report form or he may write a narrative report on his own stationery. Photocopies of records are also acceptable.

To facilitate the obtaining of medical evidence, district offices have made special contacts and arrangements with physicians, hospitals, institutions and other sources of medical evidence. If the applicant is unable to come to the district office, a district office representative will visit him at his home or elsewhere.

### **Who Makes The Disability Determination?**

The medical reports, together with the application and a report of the district office interview are forwarded to the Division of Vocational Rehabilitation (located in Hato Rey) where the disability determination is made.

In the Vocational Rehabilitation agency, each claim is reviewed by a two-man disability evaluation team which consists of a physician and a layman skilled in the evaluation of vocational aspects of disability. When determining the degree of disability, the Vocational Rehabilitation agency also decides whether the claimant has rehabilitation potential. If it is felt that the individual may benefit from vocational rehabilitation services, his case is referred to a rehabilitation counselor for consideration of his rehabilitation potential.

### **What Facts Are Needed**

Since the evaluating physician does not examine the claimant personally, he must depend solely on reports from practicing physicians for the findings on which to base his decision. The evaluating physician uses these written records as a basis for reaching independent conclusions concerning the impairment and its effect on the individual's capacity for substantial work. He can form an accurate picture of the patient's condition only if the reporting physician has given, in addition to diagnostic, prognostic and

therapeutic conclusions, the clinical and laboratory data on which he based such conclusions.

The report should, therefore, contain sufficient history to determine the date of onset and course of the disease, reports of physical findings, results of diagnostic tests, and a therapeutic history. Of special importance is information about how the impairment affects the patient's ability to perform the physical and mental functions needed for work, i.e., his ability to walk normally, to stoop or bend; to use public or private transportation; to manipulate common objects; to see and hear; to speak coherently and understandably and to perform any other activities necessary to work. An incomplete medical report often necessitates correspondence with the reporting physician for the purpose of obtaining additional information. Such recontacts place a burden on the physician and delay service to the applicant who is entitled to a speedy evaluation of his claim.

To the extent possible, the report should describe the patient's condition at the time he says he first became unable to work. This is particularly important because an applicant may lose his insured status (and thus his eligibility for benefits) unless the date he first became disabled can be medically established. The impairment must prevent work at a time when he has insured status.

### **Consultation Examinations**

About 40 percent of the disability claims filed in Puerto Rico can be decided on the basis of the information supplied by the applicant's own medical sources. In the remainder, additional evidence not available from the claimant's medical sources is needed in order to reach a sound decision. In these cases the evaluating physician in the vocational rehabilitation agency may authorize at Government expense, an independent examination and special tests from physicians in private practice. In arranging for the examination and determining the amount of the fee, the evaluating physician is guided by practices worked out between the Puerto Rico Vocational Rehabilitation Agency and the medical profession.

### **Diagnosis vs. Function**

As a rule, to evaluate the functional limitation caused by impairments, the Vocational Rehabilitation agency physician needs the same kind of history, physical findings, and laboratory data as the attending physician requires in making his diagnosis and planning his treatment. Certain medical facts, however, have greater relevance to physical capacity than to diagnosis and

therapy. For example, the results of a ventilatory study or of a calculated oxygen-consuming capacity procedure are more significant to physical capacity evaluation than to diagnosis.

About one out of every five Puerto Ricans awarded disability insurance benefits has a primary diagnosis of cardiovascular disease. If you are describing heart disease in your patient, general terms such as "mild," "moderate," or "severe" are helpful, but, unless supporting facts are included, the reviewing physician does not have the precise data he needs to assess your patient's remaining capacity for work. The medical report should include cardiac size as shown by P.M.I. and X-ray. Serial blood pressure readings in patients with hypertension are often helpful. EKG interpretations should be accompanied by descriptions and actual findings. Comments should be included as to the presence and extent of edema—as measured by physical findings, weight change with diuretics, etc. The report should also show the level of exertion that results in dyspnea and/or angina and the clinical characteristics of these symptoms.

Where dyspnea is present, it is necessary to know the characteristics of this symptom in order to accurately evaluate disability. When was it first noticed? Is it persistent or intermittent? Is it progressive? How does it relate to exercise? Dyspnea should be expressed in terms of the number of steps that can be mounted, or the distance in blocks that the patient can walk, and the speed at which these activities can be performed.

Where chest pain is the patient's principal complaint, it is important for the physician to indicate its location, whether it radiates, and how it responds to medication. The severity of angina should be related to specific activity, and circumstances; e.g., eating, walking, emotional stress, and the effects of weather conditions.

A well prepared medical report can speed the payment of disability benefits to a disabled patient. It will also avoid further requests for additional clinical or laboratory data. So by preparing comprehensive and specific clinical data for these reports, physicians can perform a great service for patients, and also save their own time.

## THE MEASUREMENT OF CORONARY BLOOD FLOW

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No experienced physician would question the significance of coronary artery disease in producing morbidity and mortality of civilized man. Because of the overwhelming importance of this disease one of the time honored goals of clinical investigators has been the study of coronary blood flow and myocardial metabolism on the reasonable thesis that this would provide better understanding of angina pectoris and related diseases. Since approximately the turn of the century methods have been available for the study of coronary blood flow.<sup>1</sup> These were first applied to the isolated heart and then as more sophisticated methods developed it became possible to study progressively more nearly physiologic situations until at present through imbedded flowmeters, coronary blood flow can be measured in alert, normally active animals.<sup>2</sup> Indeed through recent advances it is possible to follow cardiovascular activity including coronary blood flow through telemetered signals from completely unrestrained animals.<sup>3</sup> Naturally, progress in methods has not been as rapid in man as it has in experimental animals and continuous measurement of coronary flow has not become feasible. In fact the methods have been so limited that although the rate of clearance of radioactive materials injected into the myocardium<sup>4,5</sup> or the coronary circulation<sup>6,7</sup> has recently been accomplished most of the data in man to the present time have been accumulated through the use of the nitrous oxide method.

The nitrous oxide method for determining coronary blood flow<sup>8</sup> was adapted from the technique for measuring cerebral blood flow.<sup>9</sup> It depends upon the diffusion of an inert gas (nitrous oxide) from the blood stream into the myocardium until equilibrium is reached between the gas content in the coronary arterial and venous blood, and the myocardium. When this point is reached, the quantity of nitrous oxide taken up per unit weight of myocardium is assumed to be the same as that in myocardial venous blood, and hence becomes the numerator of the Fick equation. When divided by the integrated arteriovenous nitrous oxide difference throughout the saturation period (the denominator of the Fick equation) blood flow is obtained per unit weight of myocar-

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dium. Providing the arterial and venous nitrous oxide contents approach the same level, flow may also be calculated during the desaturation phase as nitrous oxide is washed out of the heart, and the same information can be obtained.<sup>10</sup> The nitrous oxide method for measuring coronary blood flow has been used extensively in experimental animals and has proven to give reasonable results in a wide variety of circumstances.<sup>11</sup> Furthermore, it has been shown to compare well with the bubble flow meter<sup>8</sup> and the rotameter<sup>12</sup> as well as the recent clearance method which follows the washout of radioactive gas.<sup>6</sup> Objective data concerning its accuracy in man are not available.

It should be obvious from the foregoing discussion that a completely satisfactory method for determination of coronary blood flow in man is not available at the present time. It is unfortunate that the more exact methods such as the ultrasonic and electromagnetic flowmeters are applicable to experimental animals, but not to man himself. The less exact nitrous oxide method, which measured integrated total left ventricular coronary blood flow, as compared to the methods for measuring flow in individual arteries, is considerably more cumbersome and does not lend itself well to the study of those situations in which anginal pain is most apt to be produced. Furthermore, it requires a steady state of finite duration and consequently transient events which might precipitate localized ischemia and pain may not be detected through its use. Although the radioactive gas clearance method<sup>6</sup> looks helpful for measuring individual coronary artery flow at the present time no complete solution appears to be available for these problems.

It may be of some interest nevertheless to survey the general varieties of information which have been obtained by the study of coronary blood flow in man even though this information has been reviewed recently.<sup>2,13,14,15</sup> Thus, for example, it has been shown that the resting coronary blood flow per unit of heart weight, the myocardial oxygen consumption, and the coronary vascular resistance are in the same general range as is found by exact methods in the dog. Coronary blood flow increases in response to those moderate degrees of exercise obtainable during cardiac catheterization. In general, diseases which reduce the left ventricular work such as mitral stenosis are associated with reduction in coronary blood flow,<sup>16</sup> whereas those associated with an increase in left ventricular work, such as thyrotoxicosis,<sup>17</sup> are associated with increased coronary blood flow and myocardial oxygen consumption. Pharmacologic agents which produce an increase in coronary blood flow in the isolated heart of experimental animals, in general, tend to produce an increase in coronary blood flow in

intact man and those which reduce cardiac output, in general, decrease coronary blood flow.<sup>2</sup>

There are some notable exceptions to this rule however, such as the nitrite "coronary vasodilators" which have long been known to be effective in treatment of angina pectoris. Although these compounds do produce dilation of the myocardial blood vessels as revealed by coronary arteriography<sup>18</sup> and although they increase coronary flow when administered preferentially into the coronary circulation<sup>19</sup> their systemic administration is not associated with an increase in coronary blood flow per unit of myocardial weight in human subjects with arteriosclerotic heart disease,<sup>20,21</sup> or in such subjects as have been reported using the recent radioactive gas clearance method.<sup>6</sup> It is also of interest that those agents which cause an increase in coronary blood flow such as dipyridamole, adenosine triphosphate, and catecholamines are known not to be effective in relieving the acute attack of anginal pain.<sup>22</sup>

Some of the more disturbing results of the study of coronary blood flow are the data which indicate that coronary blood flow per unit weight of myocardium is normal in subjects who are having recurrent episodes of anginal pain. Many investigators have been very reluctant to accept this information. However, similar data have accumulated from so many different laboratories that there appears no longer to be any reasonable doubt that it is true at least insofar as coronary flow can be measured by the nitrous oxide method<sup>14,21,23,24,25,26,27</sup> or the radioactive gas clearance method.<sup>6</sup> Calculations made from the washout of radioactive substances injected into the myocardium of subjects with atherosclerotic coronary artery disease have indicated that flow may be irregularly reduced.<sup>5</sup> Allowing for the irregular distribution of atherosclerosis in the coronary vessels, it seems reasonable that in subjects with angina there are localized ischemic areas but that the myocardium in general receives normal blood flow. Furthermore if flow falls below an acceptable lower limit in a localized area of myocardium that portion of the myocardium may be replaced slowly and painfully by scar tissue. Studies of the lactate pyruvate ratio in the coronary sinus blood have indicated that during angina in some subjects there is evidence of "excess lactate" production, which may indicate anaerobiosis.<sup>28</sup> Recently this method of calculating "excess lactate" and its significance has been questioned.<sup>29</sup> Nevertheless the opinion remains in most quarters that anginal pain is produced by a discrepancy between obtainable and desirable coronary blood flow in localized regions of the heart. It is assumed that these areas are so small in relation to the rest

of the myocardium that current methods for measuring flow are inadequate for their demonstration.

After the early woodsmen fell the giants of the forest the lesser trees become their target, and gradually, the forest is cut and then recut. Clearly some gain may be made in harvesting regrowth from the cut over areas, and there are outlying regions or points of difficult access where virgin timber still lies, but the reward per unit of labor falls progressively lower. A similar phenomenon has occurred in the 20 years that methods for studying coronary blood flow in man have been available, and the major gains took place fairly rapidly with smaller advances following in their wake. Periodically, in the course of such a long range investigation, time should be taken to survey what has been accomplished and what remains to be done. It would seem that the generally available cardiovascular pharmacologic agents have been studied sufficiently to know or predict their overall effect on coronary blood flow.<sup>2,15</sup> Whereas there will be continuing opportunities to study new agents as they are produced, in general little really new information is likely to be obtained from repeated studies of compounds which have already been thoroughly investigated. The most important common disease states have been studied, and there is sufficient uniformity in results from one laboratory to another that it is unlikely that many new concepts will be gained through repetition of studies in the usual afflictions of man. There seems little reason to believe that mass application of present methods for measuring coronary blood flow in the study of coronary artery disease would be helpful even if it were feasible, since highly detailed studies of selected individuals from the worst segment of the spectrum of coronary artery disease have shown little or no detectable difference in mean coronary flow. There would seem to be something to gain by utilizing methods from different disciplines simultaneously in the same individual. Thus it may be helpful to undertake detailed radiographic studies of the anatomy of the coronary arteries in subjects with atherosclerotic cardiac disease<sup>30</sup> combined with studies of their myocardial metabolism as revealed by standard coronary flow methods or the radioactive gas clearance method.<sup>6</sup> Valuable information may also be obtained by long range repetitive radiographic studies of the coronary arteries of the same individuals known to have coronary artery disease.

Even if methods are developed which permit continuous accurate measurement of coronary flow in man during normal activity, it is doubtful that the information derived will be basically different from that which has already been obtained in experimental animals and in man. Good methods which may easily and

safely be applied to measurement of blood flow through localized areas of the myocardium are sorely needed as are methods for measuring rates of diffusion and diffusion gradients between blood and myocardium. It is hoped that in the future investigators will be able to study more directly the interchange between the vascular system and the myocardial cell of living man.

In summary, it may be said that during the last 20 years considerable progress has been made in the measurement of coronary blood flow in man. The overall knowledge of hemodynamics of the coronary circulation has increased. The factors which control coronary blood flow are apparently very similar in the dog and in man. In the future it is hoped that good methods applicable to man will be developed for the study of flow in smaller regions of the myocardium, through diseased vessels, and into "ischemic" areas, as well as for clarification of the ultimate factors which control vasoconstriction, vasodilatation and the development of collateral circulation. Until such methods are available we would appear to have reached a comparative plateau in studies of the myocardial circulation.

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## SECCION DE RESUMENES

**EFFECT OF ETHYL ALCOHOL ON HEPATIC CIRCULATION, SULFOBROMOPHATALE IN CLEARANCE, AND HEPATIC GLUTAMIC OXALACETIC TRANSAMINASE PRODUCTION IN MAND** (Efecto del alcohol etílico sobre la circulación hepática, depuración de la bromofenolsulfoftaleína y la transamnasa oxalacética en el hombre) A.W. Childs M.D., R.M. Kivel, M.D., A. Lieberman M.D. Department of Medicine (Gastrointestinal Laboratory, San Francisco General Hospital) University of California School of Medicine, Palo Alto California. Gastroenterology 45:176 Aug. 1963.

La circulación hepática se determinó por el método del BSP en un grupo de convelecientes antes y después de la administración de una infusión intravenosa de alcohol etílico en dosis de 0.6 a 0.7 gms/Kgm de peso. Con esta dosis la concentración del alcohol en la sangre arterial 10 minutos después de la infusión era de 78-135 mgms%. Despues de la infusión del alcohol la circulación hepática aumentó en 8 de 10 casos en que fue determinada. Los cambios en el volumen sanguíneo del área esplácnica no revelaron variaciones apreciables. La presión arterial no aumentó. La concentración de la transaminasa hepática en sangre arterial y venosa no se afectó con la administración del alcohol. La depuración plasmática del BSP se redujo en 8 de 10 pacientes y era significativa entre niveles de 0.05-0.10. Esta disminución que se llevaba a cabo cuando el BSP circulaba por el hígado como resultado de el aumento en el flujo hepático sugiere una alteración de la función hepática.

MIGUEL A. SARRIERA, M.D.

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**ON HYPERTROPHIC GLANDULAR GASTRITIS, HYPERTROPHIC GASTROPATHY, AND pariETAL CELL MASS** (Gastritis glandular hipertrófica, gastropatía hipertrófica y el volumen parietal celular.) Rudolph Schindler, M.D. Department of Medicine (Gastroenterology), Loma Linda University, Los Angeles, California. Gastroenterology 45: 77-83 July 1963.

La gastritis hipertrófica se divide en tres formas principales: Intersticial, Proliferativa y Glandular. La última forma o sea la gastritis glandular hipertrófica es el tema de este reporte. En esta forma el aparato glandular aumenta de tamaño por un aumento en el número de células que componen sus glándulas. A veces se originan grietas con nódulos gigantes que fácilmente pueden ser confundidos radiológicamente con procesos neoplásicos malignos. La mucosa es normal. En muchos casos hay infiltración celular, erosiones y quistes. Sin embargo el origen inflamatorio no está completamente dilucidado. Para el autor el método más confiable para realizar el diagnóstico de las diferentes formas de gastritis hipertróficas es la toma de una biopsia quirúrgica que incluya todo el espesor de la pared gástrica. Las biopsias por succión o gastroscopia, debido a su toma superficial son de poco valor y error diagnóstico ya que las regiones profundas que están afectadas no pueden ser evaluadas porque no se hallan comprendidos en el espécimen, que es incompleto. La hipertrrofia e hiperplasia de las glándulas gástricas está frecuentemente asociada a la úlcera duodenal lo cual queda confirmado por la gastroscopia. La hiperplasia glandular adquiere mayor expresión en el síndrome de Ellison-Zollinger y la denominada gastritis gigante hipertrófica. Cambios microscópicos de inflamación se observan en las diferentes gastritis hipertróficas pero su origen es aún de naturaleza desconocida. La gastritis hipertrófica glandular es según el autor una entidad definida. Puede ser sintomática o asintomática, variando la sintomatología de grave a leve y sin cuadro clínico espe-

cífico para ella. La hipertrofia glandular se manifiesta por aumento de volumen de las células parietales e hipersecreción gástrica. La biopsia para que tenga valor, vuelven a recalcar debe ser quirúrgica comprendiendo todo el espesor de la pared gástrica. Las biopsias por succión o gastroscópicas pueden errar y no demostrar los cambios microscópicos de esta enfermedad. Tres casos con edades de 35, 71 y 54 años son presentados demostrando lo inespecífico de su sintomatología y su posible confusión con otros cuadros clínico gástricos.

MIGUEL A. SARRIERA, M.D.

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**"HEPATITIS-ENCEPHALITIS IN HUMANS WITH REOVIRUS INFECTIONS"**  
(Hepatitis y Encefalitis en el Ser Humano por Reovirus). J. A. Joske, D.D. Keall  
P. J. Leak, N. F. Stanley and M.N.I. Walter. Arch. Int. Med. 113: 8II, 1964.

La patogenicidad del reovirus en el ser humano es especulativo. Se aisló el reovirus prototipo 3 (hepatoencefalomielítico o HEV) por primera vez en 1953, de las heces fecales de un niño aborigen australiano que sufría de bronquiectasia, broncopulmonia, alopecia y conjuntivitis. Más tarde, en un niño holandés que sufría convulsiones. Desde entonces la posibilidad de que estos virus sean patógenos específicos se ha estudiado por varios investigadores. Se sabe que el virus produce cambios específicos en ratones jóvenes. Se ha descrito hepatitis, encefalitis, pancreatitis, miocarditis y miositis. El presente estudio relata tres casos en que se aisló el virus HEV en niños uno de los cuales sucumbió a la enfermedad. En éste se aisló el virus de las heces durante la enfermedad y post mortem del cerebro. Las manifestaciones principales fueron, como indica el nombre, de encefalitis en dos casos y de hepatitis en el otro. A pesar de las pruebas circunstanciales que existen es difícil ascribir ciertas infecciones al virus HEV. Sin embargo, estos tres casos demuestran que en ocasiones estos virus pueden ser patógenos.

MANUEL MARTINEZ-MALDONADO, M.D.

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**DENERVATION OF THE SPANCHNIC VISCERA** (Denervación de los Nervios Esplácnicos en el Tratamiento de Shock) Fine, Jacob, The American Journal of Surgery, 107:723, 1964.

La discusión de este artículo se centraliza en el papel que juega el sistema nervioso en el desarrollo de shock irreversible secundario a hipovolemia o a toxinas bacterianas. Hace 15 años el autor demostró en animales experimentales que el shock irreversible se podía evitar si se mantenía buen flujo sanguíneo al hígado durante shock hemorrágico. Más recientemente Lillehei obtuvo los mismos resultados mediante la perfusión de la arteria mesentérica superior de esta forma manteniendo la integridad del intestino. Hay evidencia de que tanto el hígado como el intestino son importantes en el desarrollo del shock irreversible. Durante shock el intestino libera endotoxinas que circulan hasta el hígado. Normalmente el hígado puede destruir la endotoxina, sin embargo, durante shock esta función del hígado se pierde.

En este experimento una serie grande de perros y conejos fueron sometidos a denervación quirúrgica de los nervios esplácnicos ocho semanas o inmediatamente antes de que se les produjera shock. Este procedimiento resultó en una baja en la mortalidad de un 80% en los controles a un 20% en los animales denervados.

Evitar vasoconstricción en el área esplácnica mediante la denervación no

sólo reintegra la circulación sistemática (evidenciado por un tiempo de circulación más bajo y un aumento en el rendimiento cardíaco, en el pH de la sangre y en la secreción de orina), sino que también preserva la integridad funcional del hígado, bazo e intestino.

CARLOS TORRES AGUIAR, M.D.

ACCIDENTAL ARTERY LIGATION IN HUMANS (Ligadura Accidental de la Arteria Hepática en Humanos) Brittain, R.S., et. al., *The American Journal of Surgery* 107:822, 1964.

La división accidental de la arteria hepática o una de sus ramas principales ha sido una complicación quirúrgica altamente enfatizada por varias generaciones de cirujanos debido a sus consecuencias mortales. Se sabe que algunos animales toleran bien la ligadura de la arteria hepática si se les administra antibióticos. Sin embargo, en el humano tal información no existe. Graham y Cannell luego de revisar la literatura hasta 1933 indicaron que la mortalidad secundaria a ligadura de la arteria hepática es de aproximadamente 60%.

En este artículo se presentan cinco casos de daño quirúrgico a la arteria hepática común o a la arteria hepática derecha. En cuatro de los casos fue imposible reconstruir la arteria hepática y ésta tuvo que ser ligada. No hubo evidencia clínica de necrosis hepática en ninguno de estos pacientes durante el cuidado postoperatorio. Hubo una sola muerte y ésta fue en un paciente en el cual el conducto común hepático fue también lacerado. En autopsia no se encontró evidencia de necrosis hepática y los hallazgos prominentes fueron disrupción de la anastomosis coledojejunal con formación de un absceso subhepático y la presencia de pulmonía basal bilateral.

Recomiendan los autores en casos de ligadura accidental de la arteria hepática, que siempre y cuando sea posible se trate de reconstruir la arteria. De no ser técnicamente posible, se deben dejar suficientes drenajes en el área del hígado. Por todos medios se debe evitar hipotensión y mantener una oxigenación adecuada en el paciente. Aunque el uso de antibióticos no se ha establecido como parte esencial del tratamiento, ya que el hígado humano se considera estéril, hasta tanto no haya prueba de que no son de valor alguno bajo estas circunstancias los autores recomiendan que se usen. Concluyen los mismos luego de revisar la literatura y presentar sus cinco casos, que la ligadura de la arteria hepática o una de sus ramas principales en un paciente con función hepática relativamente normal no resulta en consecuencias fatales ordinariamente.

CARLOS TORRES AGUIAR, M.D.

THE ETIOLOGY OF BRONCHOGENIC CARCINOMA (La etiología del carcinoma broncogénico) Ochsner, Alton. *Diseases of the Chest*. 45: 585-590, 1964.

El carcinoma broncogénico, muy raro hace 25 años, es ahora una de las enfermedades más frecuentes y está aumentando su incidencia más rápidamente que cualquier otra lesión cancerosa. Las estadísticas más rigurosas demuestran que esta incidencia del cáncer pulmonar sobrepasa ahora a la del cáncer de la mama y el cáncer genital de la mujer. La proporción aumentó de 3.08 por 100,000 habitantes en 1930 a 42.16 en 1955. En 1930 hubo 2,500 muertes por carcinoma broncogénico, en contraste con 40,000 en 1962 (estadísticas de Massachusetts). En 1930 el cáncer del pulmón representó sólo el 2.2% de todas las enfermedades malignas; en 1960 fue el 15%. A esta proporción, y

a menos que se haga algo para prevenirla, en 1975 será el 40% de todas las lesiones cancerosas.

No puede aceptarse que ese aumento a partir de 1930 se deba a cambios de la mucosa bronquial como consecuencia de las epidemias de influenza, muy numerosas en aquella época, como fue sugerido, sino a que, a partir de 1914 con la 1<sup>a</sup> Guerra Mundial, el hombre comenzó a fumar cigarrillos exageradamente. Así transcurrieron, hasta la década del 30, los 20 años necesarios para que los efectos cancerígenos del cigarrillo se hicieran evidentes. La teoría "influenza" fue negada por Kikuth, quien en 1925, en una serie de 249 casos de carcinoma pulmonar observados en autopsias, sólo encontró historia de influenza en 25. Por lo demás, en los últimos años la incidencia del cáncer broncogénico ha ido en aumento, al mismo tiempo que el número de pacientes con influenza ha sido infinitamente pequeño.

En cuanto al tipo de tumor, el consenso general es que el adenocarcinoma es ahora menos común que el carcinoma epidermoide y que aquellos son más frecuentes en las personas jóvenes. El Autor reportó en 1959 que entre sus pacientes de menos de 50 años de edad con carcinoma broncogénico, 44.1% padecía del tipo epidermoide y el 20.5% adenocarcinoma; entre 50 y 60 años, el 52% tenía el tipo epidermoide y 20% adenocarcinomas; sobre 70 años, el 75% era tipo epidermoide y sólo 11% adenocarcinomas.

Por otra parte, Auerbach ha asegurado repetidamente que jamás observó un carcinoma epidermoide pulmonar primario en un no-fumador. Sus trabajos demostraron también que la mucosa bronquial en un no-fumador es usualmente normal, pero aún en aquellos que sólo fuman 10 cigarrillos al día la incidencia de células anormales de la mucosa bronquial "aumenta tremendamente". Las cifras fueron:

no-fumadores -----	3.8% de células atípicas
fumadores ocasionales -----	10% " " "
10 cigarrillos al día -----	90.6% " " "
1 paquete -----	99.3% " " "
Más de dos paquetes -----	99.6% " " "

Igualmente los carcinomas *in-situ* en el bronquio variaron con el hábito de fumar:

no-fumadores -----	0
menos de diez cigarrillos al día -----	0.3%
hasta un paquete -----	0.8%
de uno a dos paquetes -----	4.3%
más de 2 paquetes -----	11.4%

Otra conclusión ha sido: una lesión del pulmón que puede ser neoplásica en un no-fumador es casi sin excepción o adenocarcinoma o no es maligna.

Estudios hechos por Doll y Hill en Inglaterra entre profesionales médicos y por la American Cancer Society en los Estados Unidos en muy cerca de 2 millones de individuos interrogados y seguidos por varios años, demostraron consistentemente que la incidencia del carcinoma broncogénico es muy baja en los no-fumadores; le siguen los que sólo fuman cigarros (tabacos, cigarros puros); después los fumadores de pipa y la más alta la proporcionaron los fumadores de cigarrillos. En cifras esto se expresa así respectivamente: 3.4, 11.4, 28.9 y 78.6 por 100,000 habitantes.

Una de las conclusiones del Real Colegio Médico de Inglaterra fue: "el riesgo de tener un cáncer del pulmón en el Reino Unido es 30 veces mayor en los que fuman 40 cigarrillos al día que en los que no fuman".

Hay, sin duda, individuos resistentes a los efectos cancerígenos del cigarrillo, así como hay otros extremadamente susceptibles.

Se supone que en 1965 morirán en los Estados Unidos más personas de carcinoma broncogénico que por accidentes de automóvil.

La curabilidad del cáncer pulmonar, en fin, es muy baja: aproximadamente un 5%. La única esperanza que podemos tener depende de lo que hagamos por evitarlo o prevenirla: la implantación de medidas para disminuir a cifras mínimas el consumo de cigarrillos.

PEDRO HERNANDEZ GONZALEZ, M.D.

## PRINCIPLES OF MEDICAL ETHICS

### P R E A M B L E

These principles are intended to aid physicians individually and collectively in maintaining a high level of ethical conduct. They are not laws but standards by which a physician may determine the propriety of his conduct in his relationship with patients, with colleagues, with members of allied professions, and with the public.

#### 1. Principles Applicable to All

There is but one code of ethics for all, be they group, clinic or individual and be they great and prominent or small and unknown. (**House of Delegates, 1934**)

#### 2. Purpose

These principles are intended to serve the physician as a guide to ethical conduct as he strives to accomplish his prime purpose of serving the common good and improving the health of mankind. They provide a sound basis for solution of many of the problems which arise in his relationship with patients, with other physicians, and with the public. They are not immutable laws to govern the physician, for the ethical practitioner needs no such laws; rather they are standards by which he may determine the propriety of his own conduct. Undoubtedly, interpretation of these principles by an appropriate authority will be required at times. As a rule, however, the physician who is capable, honest, decent, courteous, vigilant, and an observer of the Golden Rule, and who conducts his affairs in the light of his own conscientious interpretation of these principles will find no difficulty in the discharge of his professional obligations. (**Principles of Medical Ethics, 1955 edition, Preamble.**)

#### 3. Principles Apply to Members of Group or Partnership

The ethical principles controlling group practice are the same as for the individual. Since the principles of ethics for private practice absolutely forbid the splitting of fees under any and all circumstances the same rule applies to group practice and the group formed must be a real partnership in which the total income is divided not equally but according to the individual income earned by the member. (**House of Delegates, 1947**)



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by Dr. F. María Segovia de Arana

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### COMPOSITION AND CHEMICAL PROPERTIES OF OLIVE OIL

"In the chart below, taken from Hilditch (The chemical constitution of natural fats) the composition in saturated fatty acids (miristic, palmitic and stearic and non saturated (oleic and linoleic) of olive oil in various countries is shown.

#### OILS.

	Miristic	Palmitic	Stearic	Oleic	Linoleic
Italy (Tuscany)	1,1	9,7	1,0	79,8	7,5
Córcica	1,1	9,4	2,0	84,5	4,0
California	1,1	7,0	2,3	85,8	4,7
Spain	0,2	9,7	1,4	81,6	7,0
Tunis	1,1	14,7	2,4	70,3	12,2
Palestine	0,5	10,0	3,3	77,5	8,9
Greece (Rhodes)	0,4	19,7	0,3	69,6	10,4

As can be seen, olive oil, apart from containing a large proportion of a non saturated fatty acid, of twofold linkage, namely oleic acid, also contains lesser quantities of others that have more than a twofold linkage."

## **PHITOSTERINES**

"Olive oil contain "phitosterine", which, as its name indicates consists of vegetable sterines similar to the colesterine of animal fats, but with the interesting biological characteristic that they are not absorbed by the wall of the stomach and what is even more important, that they prevent, to a greater or lesser extent, the intestinal absorption of the colesterine contained in food, as has been recently demonstrated by the experiments carried out by the Chaikoff School in the United States."

## **ARTERIOSCLEROSIS AND OLIVE OIL**

"The experiments carried out by Dr. Bronte Stewart in South Africa, demonstrated that cholesterol in the blood increased when the subjects consumed animal fats, but this did not occur with vegetable fats, such as sunflower oil, olive oil, etc.

The same type of result was achieved by a group of investigators (among others, Dr. P. D. White, President Eisenhower's personal physician, and Dr. Keys) in a test carried out in Calabria and Crete on subjects whose ages varied between 45 and 65 years and the fatty part of whose food consisted almost entirely of oil. Only two out of the 657 persons examined were seen to have had heart attacks. When this group was compared with a similar one, as regards age, in the United States, whose diet largely included large quantities of animal fats, sixty cases of heart attacks were discovered.

("Time" magazine, 30 December 1957)."

## **CONCLUSIONS OF THE WORK OF DR. SEGOVIA DE ARANA**

"We must be careful and only recommend such things as can reasonably be expected to do more good than harm. In our opinion, the following measures are reasonable and well founded:

- 1) Reduce the total consumption of calories and in particular those derived from fats, to the amounts consumed, (and which quantities should be maintained) when the body weight is normal between twenty one and twenty five years of age. It is advisable to use non saturated vegetable oils in lieu of animal fats.
- 2) Take active daily physical exercise.
- 3) Avoid all excess (tobacco, alcohol, emotional tension) but such habits need not be cut down drastically.
- 4) Treat arterial hypertension if it appears."

"Through the courtesy of Torres & Ribelles, S. A., Seville, Spain, proprietors of the famous Spanish Olive Oil brand **BETIS**."

# Terramicina\*

MARCA DE LA OXITETRACICLINA

## GOTAS PEDIATRICAS premezcladas

en fórmula especial para niños

y su aliado

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preferida universalmente por los enfermos  
pediátricos y geriátricos

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a cereza silvestre

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Ambos son estables durante dos años a la  
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el frasco. Se conserva la alta potencia y la  
dosificación es siempre exacta

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ensayado y mejor comprobado, en la forma  
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por cucharadita de 5 cc.

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the *Most* active  
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of hypersensitivity may be observed occasionally. In extremely rare instances, anaphylaxis has occurred following the use of erythromycin.

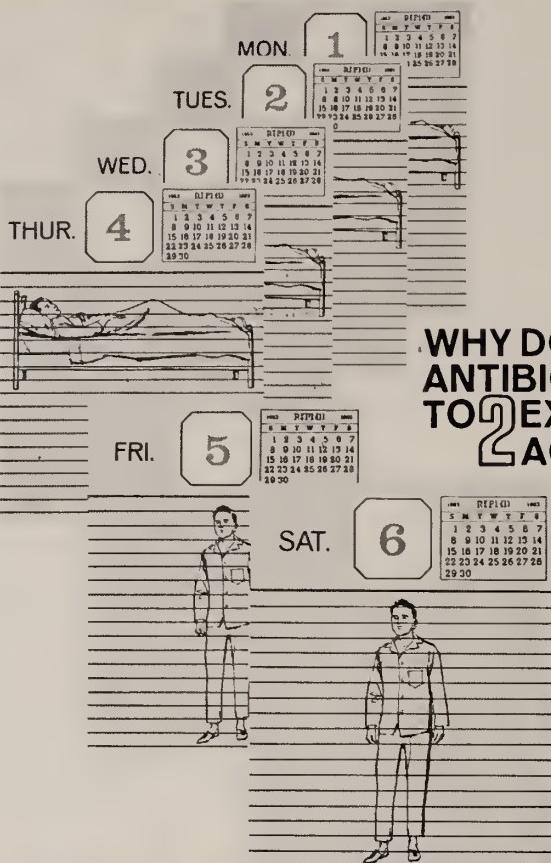
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VOL. 56

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g) Generic names of drugs should be used. Trade names may also be given in parenthesis if desired.

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i) Photographs and photomicrographs should be submitted as glossy prints, unmounted. Drawings and graphs should be made in black ink on white paper. All illustrations should be numbered (Arabic) and top indicated. A legend should be given for each and its location should be indicated in the text. A maximum of 6 illustrations is allowed without cost to the authors.

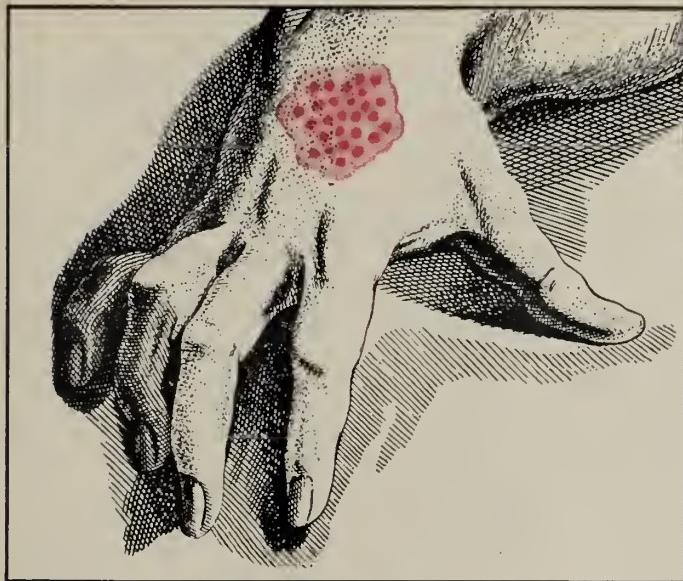
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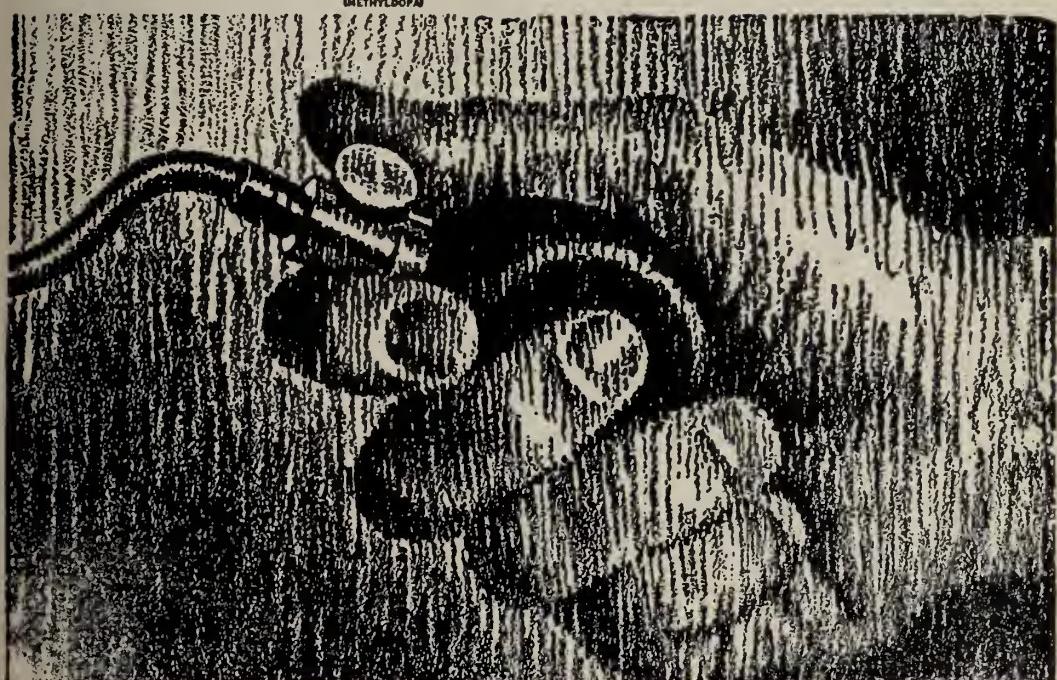
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**References:** 1. Peele, J. C.: Med. Times 86:1228 (Oct.) 1958. 2. Riddle, A. C., Jr.: Oral Surg., Oral Med., Oral Pathol. 8:617 (June) 1955. 3. Lamphier, T. A.: Clin. Med. (Dec.) 1962.

# hypertension

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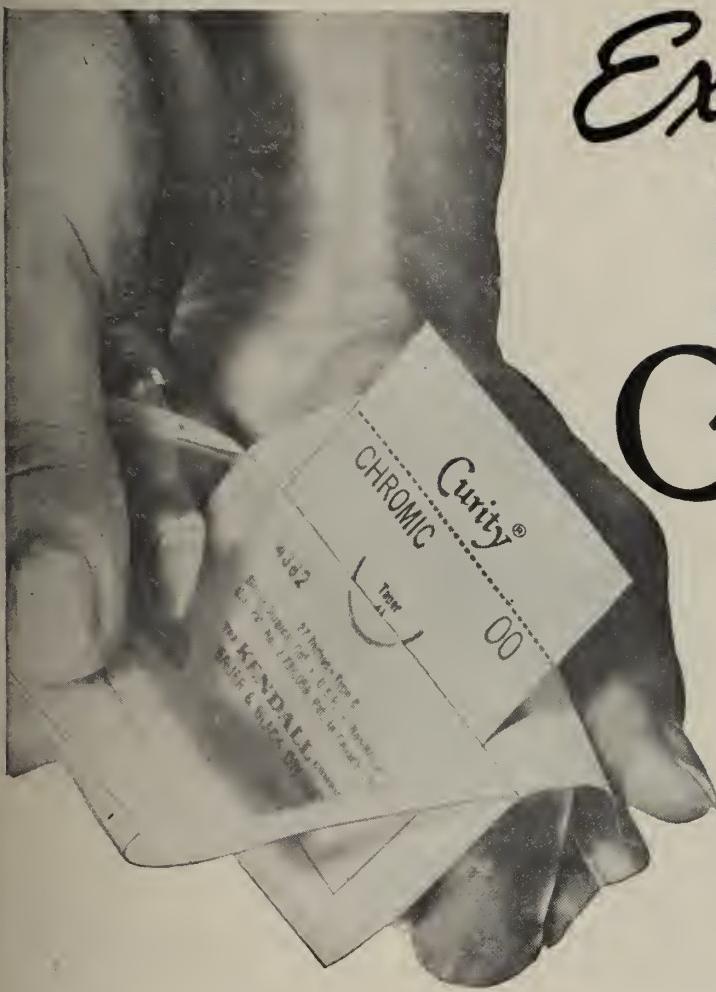
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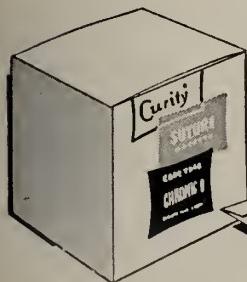


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## As Shown in Two New Controlled Studies:

**Lieberman, A., and Guglielmelli, S.: Persantin—A Double Blind Study. Angiology 15:290, 1964.**

**Method:** A total of 128 hospitalized patients, the majority in severe congestive failure, were studied. Most were 40 to 60 years old. Fifty-nine received dipyridamole, 25 mg. q.i.d., and 69 received placebo tablets q.i.d., for 2 to 3 months in most cases. Routine therapy was continued as needed in both groups.

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**Neumann, M., and Luisada, A. A.: Effect of Rapid- and Slow-Acting "Coronary" Drugs on Precordial Pain of the Aged. Am. J. M. Sc. 247:156, 1964.**

**Method:** In a double-blind study, 33 elderly patients with chronic angina pectoris received placebo, dipyridamole 50 mg. t.i.d., and other coronary drugs, each for a 6-week period. The number of nitroglycerin tablets consumed in the last 2-week period was compared for each test preparation.

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1. Griep, A. H.: A Long-Term Therapy of Ischemic Heart Disease. Angiology 14:484, 1963. 2. Wirecki, M.: Dipyridamole: Evaluation of Long-Term Therapy in Angina Pectoris. Current Therap. Res. 5:472, 1963. 3. Gaddy, C. G.: Long-Term Treatment of Myocardial Ischemia. Virginia M. Month. 91:155, 1964. 4. Griep, A. H.: Nocturnal Angina Pectoris. GP 29:78, 1964. 5. Wheatley, D.: Prophylactic Drug Therapy of Angina Pectoris in General Practice. Proc. Fourth World Congress of Cardiology IVB:130, 1962.

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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



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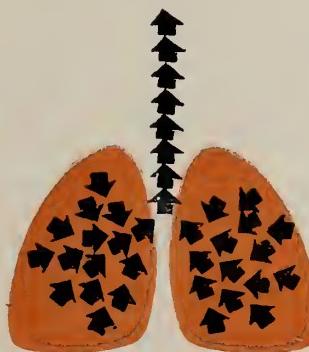
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**INJECTABLE:** Each cc. contains medroxyprogesterone acetate, 50 mg. Also: Polyethylene Glycol 4000, 28.8 mg.; Polysorbate 80, 1.92 mg.; Sodium Chloride, 8.65 mg.; Methylparaben, 1.73 mg.; Propylparaben, 0.19 mg.; Water for Injection q.s. Supplied in 1 cc. vials.

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**CAUTIONS:** No significant untoward effects or intolerance. Animal studies show Provera (medroxyprogesterone acetate) possesses adrenocorticoid activity and produces some instances of female foetal masculinization. Neither of these effects has been observed in human beings, but the possibility should be considered under conditions of prolonged high dosage.

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**Precautions:** Anuria.

\*From clinical data on file at Lederle Laboratories. Posed by model.

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## LYMPHANGIOGRAPHY IN PRIMARY LYMPHEDEMA

A PRELIMINARY REPORT

RAFAEL G. SORRENTINO, M.D. F.A.C.S.

JOSE T. MEDINA, M.D.\*

Kimmoth<sup>1</sup> originally devised lymphangiography for the investigation of lower limb lymphedema. In recent<sup>2,3</sup> years various attempts have been made to outline the lymphatics with the intra-lymphatic injection of oily contrast media for the purpose of opacification of the lymph nodes. It was hoped with this method to detect subclinical lymph nodes metastasis. It soon became evident that this procedure for such a purpose has a limited value and many workers abandoned this technique as useless, limiting it only for the study of lymphoma. Another drawback in the use of oily contrast agent is the relative frequency of embolic manifestations. Recently<sup>4,5</sup> the value of lymphangiography in the study of lymph flow and lymphatic dynamics has been emphasized. It is the purpose of this communication to present our experience with patients having primary lymphedema of the lower limbs in an attempt to demonstrate lymphatic abnormalities in the dynamics and morphology of the peripheral lymphatic system.

### Technique

F. D. C. blue dye 10% (Fouguera) mixed with procaine has been used. Half cc. of this solution is injected into the interdigital space between the first and second and the second and third toes. After an elapsed period of 30-60 minutes, a transverse incision is made on the dorsum of the left foot over the lymphatics visible under the skin. (Figures 1 and 2). A suitable lymphatic is isolated. 50% Hypaque is the opaque medium used in our cases which is injected by means of a number 27 hypodermic needle attached to a suitable polyethylene tube catheter (Figure 3). Ten

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\* Assistant in Radiology.



FIGURE 1

The absorption of the blue dye by the lymphatics 30-60-minutes after inyection is demonstrated under the skin.



FIGURE 2

The transverse incision over the dorsum of the foot after local infiltration with an anesthetic agent is illustrated.

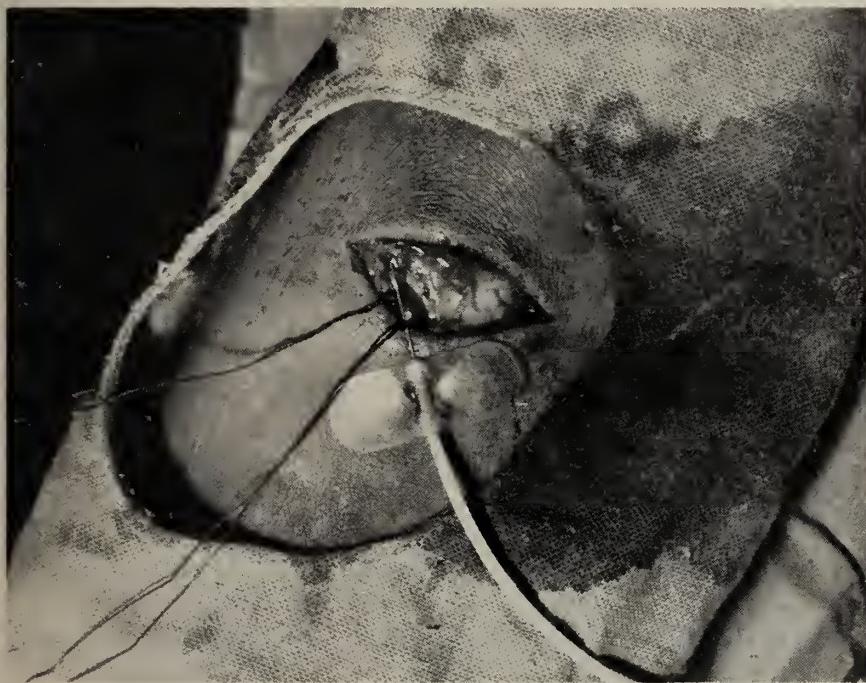


FIGURE 3

Catheterization of the lymphatic by means of a number 27 hypodermic needle attached to a fine polyethylene catheter is shown.



FIGURE 4  
Closure of the skin.

cc. of the contract agent is injected very rapidly, the patient experiencing a transitory, excruciating pain when the contrast agent is well injected into the lymphatic. Radiographs of the entire limb and pelvis are taken in rapid succession. At the end of the procedure the skin is closed by means of fine interrupted suture (Figure 4).

### Material

Twenty patients with primary lymphedema have been studied, mainly in the second and third decade. In 50% of the cases, the lymphatics could not be cannulated. The main reasons for the failure were the extensive hypoplasia of the lymphatics in some of these patients and the degree of fibrosis of subcutaneous tissue on patients with lymphedema of long duration. In cases with long standing lymphedema with fibrosis of the subcutaneous tissue persistent bleeding was encountered with poor hemostasis, making



FIGURE 5

The normal distribution of lymphatics below the knee is shown.

the procedure very difficult. There were no complications and all patients withstood the procedure very well.

### Discussion

In order to appreciate alterations in lymph flow and lymphatic channels, the normal roentgen anatomy should be understood. The normal lymphatics parallel the veins throughout the body. In the lower extremities they accompany the greater and lesser saphenous veins. In the peripheral regions, one will usually see only one or two free caliber channels. Near the inguinal region an increasing number of lymphatics will appear and one may see 4-8 channels leading into the first group of nodes (Figures 5, 6, 7, 8). The number of lymphatics seen below the knee will depend on whether the lateral or medial distribution is opacified. Flow through the



FIGURE 6

Distribution of lymphatics along the medial aspect of the thigh is demonstrated.



FIGURES 7, 8

Several channels leading to the inguinal nodes is illustrated.



lymphatics is extremely rapid. The inguinal nodes will fill within 1-5 minutes following the injection.

Kimmoth<sup>1</sup> divided lymphatic abnormalities into four types. 1—Hypoplasia was the most common finding. 2—Dilated or varicose channels were frequently associated with dermal backflow, where in many collaterals channels were filled into the skin. 3—Aplasia of the lymphatic was a rare occurrence. 4—Dermal backflow also was seen in a small percentage of the cases.

Kimmonth postulated that lymphatics might not manifest themselves in patients with lymphatic abnormalities unless there was a superimposed trauma, an infection, radiotherapy or surgery.

Collateral circulation as manifested by dermal backflow can be present with or without obstruction. Following obstruction, extensive collateral circulation must be established to maintain lymph flow for, if this is inadequate, the system decompensates and edema results.

Figure 9 A, B is a case of lymphatic hypoplasia with dermal reflux in a patient with primary lymphedema. In figure 10 the external appearance of the skin is illustrated in a patient with hypoplasia and extensive dermal reflux. Considerable dermal backflow is demonstrated in fugure 11 where a solitary tortuous lymphatic is shown with extensive collateral channels. The solitary lymphatic visible is feeding dermal collaterals. In one patient there was complete aplasia of the lymphatics. No lymphatics could be made visible after several interdigital injection of the diffusible dye.

In the group of patients studied, the most frequent lymphatic alteration demonstrated was the presence of dermal collaterals or dermal reflux. This was demonstrated both clinically and radiographically, the area of dermal reflux seen in the roentgenograms being visible clinically as a pool of blue stained tortuous lymphatics with erratic distribution in the medial aspect of the lower extremity, most frequently in the lower portion. In many instances the lymphatics could not be cannulated because of the presence of marked hypoplasia. Sometimes the only lymphatic visible was injured and the procedure had to be cancelled. In some cases a lymphatic was not visible, the only manifestation of the abnormality being the presence of considerable dermal reflux. In one case the lymphatics were more numerous than usual and the only clue as to the presence of an abnormality was the presence of slight dermal reflux and tortuosity of the lymphatics. In our series, the most frequent abnormalities encountered were hypoplastic lymphatics with dermal reflux, sometimes associated with varicose tortuous trunks.



FIGURE 9 A, B

Patient with unilateral lymphedema with the demonstration of lymphatic hypoplasia and dermal reflux.





FIGURE 10

Demonstration of the external appearance of the skin in a patient with extensive dermal reflux.



FIGURE 11

Considerable dermal backflow is demonstrated with a solitary lymphatic filling dermal collaterals.

## SUMMARY

Twenty five patients with primary lymphedema were studied. Alterations on lymphatic flow and on the normal anatomy of the lymphatics were encountered. The most frequent abnormalities were hypoplasia of lymphatic trunks with dermal reflux, and varicose trunks. The presence of collateral circulation as manifested by dermal backflow is an index of the attempt of the lymphatic channels to maintain lymph flow.

## RESUMEN

Se estudiaron 25 pacientes con linfedema primario encontrándose alteraciones tanto anatómicas como de circulación a nivel de los linfáticos de las extremidades afectadas. Las anomalías más frecuentemente encontradas consistieron en hipoplasia de los troncos linfáticos con reflujo dermal y troncos varicosos.

La presencia de reflujo dermal podría interpretarse como un intento del sistema linfático alterado para mantener el flujo linfático por vía de un sistema colateral.

En aproximadamente la mitad de los casos se fracsó en el intento de cateterizar los linfáticos debido a las anomalías arriba descritas.

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## CARCINOMA OF THE MALE BREAST

GUILLELMO E. ARAGON, M.D.

### Incidence

The relative infrequency with which the average practitioner and, indeed, the average surgeon observes carcinoma of the male breast oftentimes results in errors in diagnosis or costly delays in establishing treatment.

Because of the rarity of the disease, many patients themselves fail to associate in their minds the presence of a mass in the breast with a serious cancer. Certainly, they fail to do so with the same frequency as the better informed female population. The consequence of this lack of information among the general male population has been the unfortunate delay which is observed in all studies of male breast carcinoma.

In Treves and Holleb's<sup>1</sup> series of 146 male breast cancers, the median duration of symptoms before the first medical consultation was sought was nine months; 13% of patients had in fact had their tumor four years or more. In Wainwright's series, the average duration of the tumor at the initial examination was 2.7 years. In Moss' series<sup>2</sup> of 481 microscopically confirmed male breast cancers, the average delay was five months.

Besides ignorance, fear is unquestionably a most important factor in this unfortunate delay.

To compound the picture, the physician oftentimes is responsible for further procrastination. In Moss' series, one out of every ten physicians failed to act promptly when confronted with a breast lesion later proven to be a carcinoma.

The incidence of carcinoma of the male breast in all major series, i.e.: Haagensen's,<sup>3</sup> Wainwright,<sup>4</sup> Treves,<sup>5</sup> is somewhat less than 1%. Moss' statistical series—which is by far the largest—shows an incidence of 0.9% or 1 male breast CA per 110 female breast cancers. The median age of these patients is 51 years against 64 for the female form.

As in its female counterpart, family history of female breast cancer is important as it bears a definite relationship to the incidence of male breast carcinoma.

### Etiology

Haagensen's series discloses a history of trauma in 12% of

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the cases but Treves has been unable to find definite correlation between carcinoma of the male breast and previous trauma.

The German literature<sup>6</sup> contains many suggestions of a possible relationship between carcinoma of the male breast and gynecomastia among starved males during the war. Yet, whether such relationship actually exists is open to question as in no instance has there been a report of transition from histopathologically confirmed gynecomastia to subsequent malignancy. Schottenfeld and Lilienfeld<sup>7</sup> categorically state that "no satisfactory estimate of the relative prevalence of gynecomastia to male breast cancer has been made from the highly selected series of cases observed in medical institutions." Carcinoma of the breast is known to occur with greater frequency in patients on long-standing estrogen therapy for carcinoma of the prostate. Graves and Harris<sup>8</sup> have emphasized this point and presented a case successfully resected while the disease was still confined to the breast.

### Symptomatology

The most common single symptom is a breast mass. In Treves series, a mass was noted in 105 of 132 cases or an incidence of 67%. Nipple discharge, alone or in conjunction with a mass, was present in 10% of the cases. Nipple retraction, the next most common symptom, was present in 8.5% of cases. Ulceration occurs somewhat earlier than in the female as does fixation to the chest wall and axillary metastasis. Pain as an early occurrence is conspicuously absent. Carcinoma of the male breast forms a hard, poorly delimited mass underneath the nipple or areola. Nipple changes which are quite common, such as retraction or ulceration, are due to proximity of the mass. As the disease progresses, it also narrows the areola and appears on the surface in the form of small nodules surrounding or invading the areola.

The disclosure of a mass in the adult male breast warrants suspicion of a malignant tumor. When the mass is associated with a nipple abnormality, the diagnosis of cancer is almost assured. In either case immediate biopsy is indicated. Invasion of the pectoralis muscles by tumor occurs early since they lie in quite close contact. Extensive metastases to axillary lymph nodes are present in better than 50% of the cases. Bilateral involvement does occur in 1-2% of the cases as compared to an incidence of 8-12% in the female.

### Differential Diagnosis

In the very young adult, adolescent type of hypertrophy of

the breast should be considered. This condition in reality causes no major problem as it presents a typically discoid, movable, somewhat tender mass during puberty. True gynecomastia, which occurs in the late teens or early twenties, produces a larger and softer breast which mimics the female gland. Hypertrophy of the male breast due to liver or thyroid disease may form a movable, somewhat tender tumor beneath the areola. Carcinoma of the male breast is so rare before the age of 30 that there is no justification for biopsying tumors in these younger patients. Their benign nature is apparent, moreover, from their physical character.

In males past 50, carcinoma has to be distinguished from the senile type of benign hypertrophy of the breast. This benign condition begins as a tender, small, discoid mass beneath the areola which is very well delimited, rounded and movable and exhibits tenderness which is out of all proportion to its small size. Carcinomas, on the other hand, are usually poorly delimited and somewhat firm and not ordinarily tender. The tenderness of senile hypertrophy usually diminishes after two or three months and the tumor will disappear after six months. If a true mass is present and the diagnosis proves difficult on clinical grounds, mammography may be of help.

### Pathologic Classification

Every type of tumor seen in the female may be found in the male breast. Carcinoma of acinar origin, however, occurs with considerably less frequency than the 5% incidence seen in the female.<sup>9</sup> In contradistinction, carcinoma of ductal origin occurs more commonly than in the female. Moss' series of 507 cases presented the following types of tumors. (TABLE #1)

TABLE I  
TYPES OF NEOPLASM IN 507 CASES OF MALE BREAST CARCINOMA  
(MOSS' SERIES)

Page's Carcinoma	1
Cystosarcoma Phyllodes	1
Lymphoma	}
Sarcoma	13
Liposarcoma	}
Ductal Carcinoma	492
	<hr/>
	TOTAL
	507

Median Age — 54 (64 for Female)

### Prognosis

The prognosis is proportionately less favorable in the male

than in the female for the reasons stated earlier, namely, reluctance to see the doctor or delay in establishing a diagnosis. Only 33% of the cases in Moss' series were diagnosed while the tumor was localized to the breast in contrast to 44% for female type of breast carcinoma.

When surgery alone was used, 41% of males with carcinoma in all stages as against 50% in females survived 5 years. When the disease was localized to the breast, the 5-year survival in males was 59% against 72% in females. When there were regional metastases, 39 of males and 42% of females survived 5 years. Radiation as an adjunct to radical mastectomy does not seem to improve the picture substantially.

Using a combination of therapeutic modalities, the 5-year survival in all stages of male breast carcinoma remained at 41% as against 44% for female breast cancer. In male breast carcinoma localized to the breast, 50% survived 5 years as compared to 67% for the female. When the lesion was accompanied by regional metastasis, the 5-year survival figures were 44% and 41% respectively. According to Treves,<sup>10</sup> evidence does seem to indicate that the critical period in male breast carcinoma is the first five years after surgical therapy and that many patients will continue to do well once they have passed the five year mark.

### Treatment

The treatment of choice for an isolated breast lesion or a breast lesion with regional axillary metastasis remains the standard Halstedian radical mastectomy. Skin grafts must be resorted to with considerably more frequency than in operating the female breast, but this presents no particular problem as most grafts do take quite well against the thoracic cage. (FIG. #1)

A high percentage of cancers of the male breast with distant metastasis or with recurrent carcinomas after operation seem to respond well to orchietomy. However, the clinical response to orchietomy cannot be predicted from the pathological type of the primary breast tumor; neither can the effect of the gonad ablation be foretold by the structure of the testis. The addition of estrogenic therapy to orchietomy has proven generally disappointing. Its greatest use is in conjunction with radiotherapy in the advanced carcinoma with ulceration.

More recently, a host of clinicians, among them Dao,<sup>11</sup> D'Alessandro,<sup>12</sup> Cade<sup>13</sup> and Douglas, have advocated adrenalectomy for relapse following orchietomy, generally with good results. Treves,<sup>10</sup> who is not generally convinced of the merits of adrenalectomy, has argued against this type of ablative surgery basing his argument upon the fact that neither the estrogens disappear after

adrenalectomy nor is one assured of complete removal of the adrenals, as Graham at Memorial Center has demonstrated accessory adrenals in 32 of 100 consecutive autopsies. This would seem to reinforce the case for hypophysectomy but, as matters now stand, adrenalectomy and hypophysectomy for the treatment of male breast carcinoma probably need further elucidation.

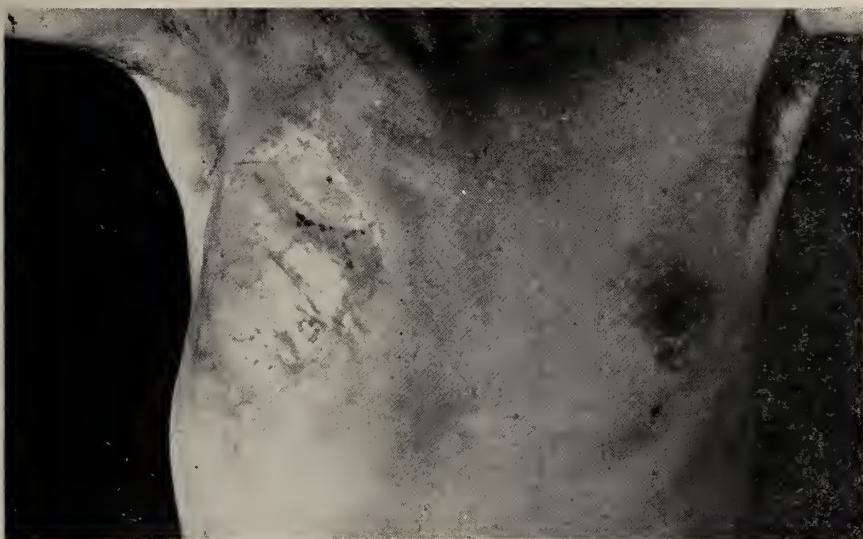


FIG. I.—Large skin graft secured with electric dermatome at .0014" with 100% take (Case B).

#### CASE PRESENTATIONS

##### Case #1

Patient F. O., an 80 year old arteriosclerotic male, was admitted to the Veterans Hospital September 13, 1962, with a chief complaint of a lump in the right breast of 2 weeks duration. The mass was slightly painful but non-tender to palpation. The veracity of the history, however, was dubious as to duration of symptoms due to the patient's advanced cerebral arteriosclerosis. Past history and review of systems were non-contributory. On physical examination, he presented a 6 x 5 x 2 cm. mass in the central region of the right breast fixed to the skin beneath the nipple and to the thoracic wall. There was a second mass which was hard and non-tender and measured 1 cm. in diameter and was located in the anterior group of right axillary lymph nodes. A needle biopsy was performed 4 days after entering the hospital and the diagnosis of carcinoma of the breast with metastasis was thus verified. Two days later, the case was presented to the Tumor Board where it was the consensus of opinion that in view of the

advanced stage of the patient's disease he should best be treated with radiotherapy.

### Case #2

Patient S. R., a 33 year old penal guard, was apparently in excellent health until the middle of September 1954 when one morning, upon arising, he experienced pain in the left breast. Two days later, he noticed a milky discharge. Alarmed, he went to see a physician who sent him home to rest for two weeks. As the breast pain and nipple discharge persisted, he was finally referred to our hospital. There was no history of trauma.

On physical examination he appeared to be a well developed, well nourished young male whose only positive findings were limited to his left breast, where a tiny opening was evident at the apex of the nipple. Although no mass was present, pressure in the subareolar area produced a milky discharge through the opening in the nipple. There were no axillary masses present. The rest of the physical examination as well as the laboratory and X-ray data were non-contributory. Soon after admission the patient was seen by a surgical consultant who palpated enlarged lymph nodes on both axillae and recommended simple excisional surgery of the nipple and areola and biopsies of both axillae. On October 28, 1954, the patient was taken to the operating room where, under general anesthesia, a simple mastectomy and bilateral lymph node biopsies were performed. Pathological report of both axillary biopsies revealed reactive hyperplasia. Slide examination of the main specimen revealed non-infiltrating duct cell (or comedo) carcinoma. (FIG. #2) Accordingly, on November 11, 1954, the patient underwent a left radical mastectomy. Histopathologic examination of the submitted specimen failed to reveal any evidence of carcinoma. Actually this tumor, which was well localized and exhibited no metastasis, had been excised in toto in the course of the simple operation. When last seen, quite recently, the patient presented no evidence of recurrence.

### Case #3

Patient H. C. is a 53 year old white male who, four months prior to admission, noticed a firm, non-tender nodule in the left breast. The mass had increased slowly in size up to the time of admission on February 13, 1963. On examination, the breast exhibited an irregular mass in the central area which measured 2-1/2 x 4 cm. and was not fixed to the chest wall. The nipple was retracted. There were several enlarged, firm, non-tender regional

axillary metastases, the largest one of which was located in the anterior group and measured 2 cm. in diameter. Laboratory data was non-contributory. Mammography was read as indicative of carcinoma of the left breast. (FIG. #3). Bone surgery including chest, skull, cervical and dorsal spine, pelvis, and both femora was negative. Six days later, patient underwent a standard left radical mastectomy after frozen section biopsy revealed infiltration.

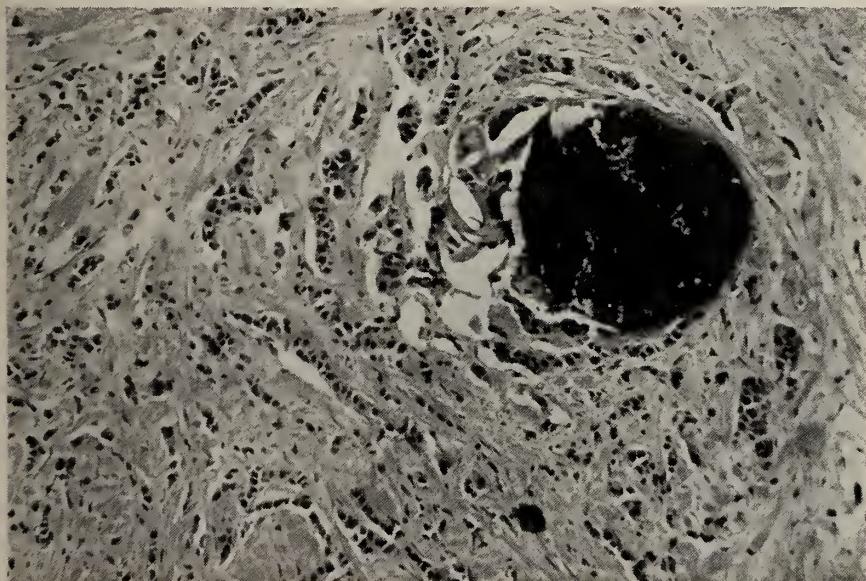


FIG. II—Intraductal carcinoma without parenchymal invasion (Case No. 2).

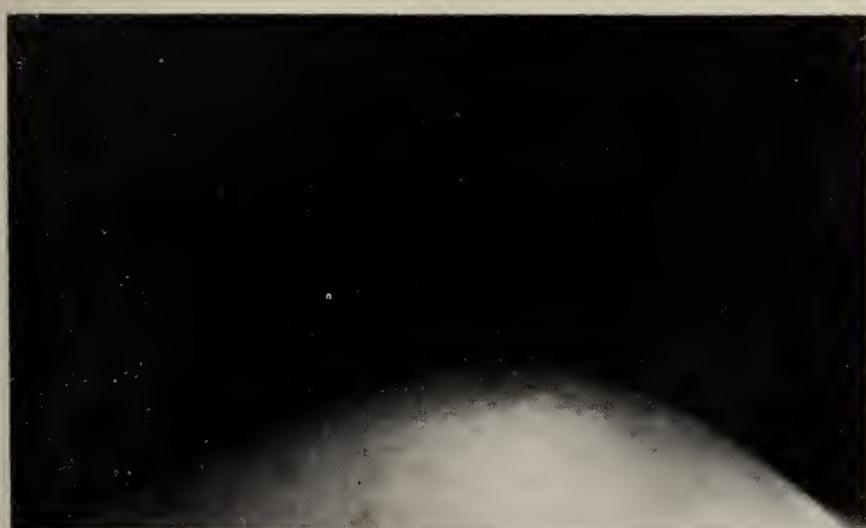


FIG. III—Mammography revealing typical specks of microcalcification (Case No. 3)

ting duct cell CA. (FIG. #4). A skin graft from the left thigh was used to cover the large anterior pectoral skin defect. The pathological report revealed 28 positive axillary lymph nodes out of a total of 34. Postoperative convalescence was uneventful. Following surgery, the patient underwent a course of irradiation to the axilla, supraclavicular and internal mammary regions. When last seen, in April 1964, he showed no evidence of recurrence.



FIG. IV—Typical infiltrating duct carcinoma with microcalcification  
(Case No. 3)

#### SUMMARY

1. Male breast carcinoma is rare, occurring with a 0.9% incidence.
2. The disease is usually diagnosed late: in 67% of the cases the diagnosis is established when the tumor is no longer localized.
3. Patients and physicians must be alerted to reduce the fatal lag before the diagnosis is established.
4. The salient points in diagnosis and treatment have been stressed.
5. Three cases have been presented exemplifying different stages of the disease and modalities of therapy.

#### SUMARIO

1. Carcinoma de la mama ocurre raramente en el varón, presentando una incidencia de únicamente un 0.9%.
2. El diagnóstico se establece tardíamente por lo general:

67% de los casos se diagnostican cuando la enfermedad ha dejado de estar localizada.

3. Es necesario recalcar ante pacientes y doctores los puntos salientes de la enfermedad para evitar la tardanza fatal con que se establece el diagnóstico.

4. Se han enfatizado los puntos principales del diagnóstico y del tratamiento.

5. Se presentan tres casos clínicos representativos de diferentes manifestaciones de la enfermedad y formas de tratamiento.

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## SURGICAL TREATMENT OF MITRAL VALVE DISEASE

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Mitral valve pathology and its surgical correction may be divided into two main groups; stenosis and insufficiency. The former has not been a great problem while the latter has been a challenge to all surgeons. It was not until a few years ago that the treatment of mitral insufficiency came to a plateau with the recent development of the ball valve prosthesis.

Surgery of the mitral valve has followed a series of stages<sup>1</sup> which portray very well the dynamic development of cardiovascular surgery. There was an experimental stage at the beginning of this century during which MacCallum and McClure, who deserve special mention, demonstrated the physiological effects of experimentally produced mitral stenosis and insufficiency (1903). The following year, Haecker and Cushing and Franch reported successful attempts at producing mitral insufficiency in the dog. In 1909, Bernheim produced mitral stenosis by means of a ligature placed around the base of the mitral orifice. In 1913, Doyen attempted to section a stenosed mitral valve. In 1923, Cutler, Levine, and Beck reported their disappointing experience with the surgical treatment of mitral stenosis. On May 20, 1923, they undertook their first clinical case. A tenotomy knife was passed into the left ventricle and attempts were made to incise both cusps of the stenotic mitral valve. The patient lived four and one half years after operation and died of pulmonary congestion secondary to an iatrogenic mitral insufficiency. That same year, Allen made an unsuccessful attempt using a cardioscope. This patient died before any definitive surgery could be accomplished. Between 1923 and 1928, Cuttler and associates operated upon six additional patients but all succumbed. In 1925, Souttar successfully dilated a stenosed mitral valve by inserting his finger through the left atrial appendage. His success was not well appreciated and apparently he did not feel strongly enough about its advantages so as to repeat the same procedure. Thus, it was 20 years later that Bailey employed this approach. In 1948, Bailey, on his fifth at-

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tempt, and Brock and Smithy, working independently, succeeded in performing a successful "mitral commissurotomy".

In 1948, Sweet and Bland in America and d'Allaines and associates in France devised and carried out a decompression of the hypertensive pulmonary circuit in mitral stenosis by means of an anastomosis between the cardiac end of a branch of the right superior pulmonary vein and the azygos vein, while Bailey and Harkin produced an atrial septal defect for decompression. This method had been suggested by Jarotsky in 1926.

It was in May of 1953 that John H. Gibbon<sup>2</sup> performed and reported the first successful intracardiac procedure under direct vision using cardiopulmonary bypass. On March 26, 1954, C. Walton Lillehei<sup>3</sup> and associates, using cross circulation based on the Andreason and Wattsons azygos flow, operated the first of forty-five patients all with complex types of intracardiac pathology. For the first time ventricular septal defects, atrioventricularis communis, and tetralogy of Fallot were completely corrected during cardiotomy. These two dates marked the opening of a new era in cardiac surgery; "the walls of the heart could be opened at last". This lead many investigators to devise many approaches for the correction of mitral insufficiency. Glover, Lillehei, Varco, Kay, Gerbode and many others described plastic procedures to correct mitral insufficiency which ranged from pericardial tubes to vein grafts, tendon grafts, rigid and mobile Ivalon sponge slings, lucite baffles, artificial leaflets, and narrowing of the mitral annulus among others. These techniques were unsatisfactory and thus valve replacement was considered as the probable solution to this problem. In 1961, Harken and Starr successfully replaced the aortic and mitral valve with a ball valve. The ball valve prosthesis was further developed by Starr<sup>4</sup> and Edwards and, since then, it has had world wide acceptance as an artificial substitute for the mitral valve.

The long term results obtained on patients who underwent closed mitral commissurotomy plus the low morbidity associated with cardiopulmonary bypass indicated to most surgeons the advisability of correcting mitral stenosis under direct vision. This trend we have come to accept as the logical recourse in this serious affliction. This report describes our experience with patients who have undergone open mitral valve surgery.

## I. Clinical Materials

The patients were admitted and operated upon between August 1, 1963, and July 1, 1964. All had acquired mitral valve disease secondary to rheumatic fever. There is a total of nine

patients of whom three underwent open mitral commissurotomy, and six underwent total replacement of the mitral valve with the Starr-Edwards Ball Valve Prosthesis.

#### A. Mitral Commissurotomy

Three patients had severe mitral stenosis and underwent open mitral commissurotomy. All were females and their ages were: 16, 16, and 42 years.

The average age was 24.7 years. The etiology of the diseased mitral valve was rheumatic fever at an earlier date. The patient who was 42 years old had aortic insufficiency which was not diagnosed preoperatively. All these patients had right ventricular hypertrophy in electrocardiogram or vectocardiogram. All except one (42 years old) had normal sinus rhythm preoperatively. They all had symptoms and fell in Class III to IV according to the American Heart Classification.

#### B. Mitral Valve Replacement

Six patients were operated upon for total replacement of the mitral valve. Of these, two (33%) were females and four (67%) were males. The average age for males was 38 years, that for females 25 years, while the overall average age was 31.5 years.

As with the previous group, the origin of the mitral valvular disease seemed to be predominantly rheumatic fever with secondary valvular damage. Two patients also had a severely calcified mitral valve. The six patients had more symptoms and more dyspnea on effort than those of the previous group. All patients except one were in normal sinus rhythm pre and postoperatively. The one patient with atrial fibrillation was electrically converted (D.C.)\* as an elective procedure postoperatively. The predominant lesion in four patients was mitral regurgitation and mitral stenosis in the remaining two. One of these two patients had a severely calcified mitral valve while the other had a fibrosed non-elastic valve.

### II. Pre-operative Evaluation

On admission, careful attention was paid to the symptoms of cardiac decompensation or impending decompensation. Routine blood chemistry was done and whenever indicated liver function or/and renal function tests were ordered. Electrocardiography,

\* With the Direct Current Cardioverter. One shock at 100 Watts/sec.

TABLE 1

Name	Age	Weight (kgs.)	Date of Surgery	Priming volume and Solutions	Duration of Perfusion	Lowest Temp. (Co)	Plasma Hemoglobin mg.s. %**	Size of Starr-Edwards Prosthesis
1. O. V.	35	56.8	7/15/63	1,000 cc Blood	1 hr. 16 min.	25.0°	-----	#3 M
2. I. L. O.	46	60	8/1/63	1,000 cc 5% D/W	1 hr. 28 min.	26.5°	-----	#2 M
3. R. G. S.	23	47.2	1/16/64	1,000 cc L.M.W.D.*	1 hr. 38 min.	29.0°	-----	#3 M
4. V. H. C.	39	57.3	1/24/64	1,000 cc Blood	1 hr. 28 min.	23.5°	66 mg. %	#3 M
5. T. A.	28	50.9	4/2/64	1,000 cc L.M.W.D. 100 cc Mannitol 25%	1 hr. 45 min.	29.0°	52 mg. %	#3 M
6. M. V. V.	33	58	4/10/64	1,000 cc L.M.W.D. 100 cc Mannitol 25%	1 hr. 30 min.	28.0°	27 mg. %	#4 M

\* 10% Low Molecular Weight Dextran (Rheomacrodex, Pharmacia)

\*\* Immediately post perfusion.

vectorcardiography, chamber analysis (X-rays), phonocardiogram, and total blood volumes ( $I^{131}$ ) were done on all patients. The blood volume was very useful as a baseline for subsequent fluid and blood replacement postoperatively. Intensive medical management was given pre-operatively, consisting of restricted activity, digitalis, diuretics and low salt diet (500 mgs.)

### III. Operative Procedure

All patients were operated upon with the De Wall-Lillehei type oxygenator and the Zuhdi heat exchanger. The three patients who underwent a mitral commissurotomy had a right postero-lateral thoracotomy through the bed of the 5th rib. Three patients with total mitral valve replacement had the same approach, while the remaining three underwent a left postero-lateral thoracotomy. In the first case, the oxygenator was primed with 5% Dextrose in water and with whole blood in the second case. In the last seven cases, low molecular weight dextran<sup>5\*</sup> prime only was used (20-25 cc/kg. body weight). Mannitol was added to the priming volume in order to enhance diuresis during and after cardiopulmonary bypass (12.5 to 25 grams).

Heparin was used to prevent coagulation during cardio pulmonary bypass (3 mg./kg. body weight) and Polybrene was given to neutralize the effect of heparin (6 mg./kg. of body weight). Epsilon amino caproic acid<sup>6</sup> was routinely used in the last seven cases (15 mg. 100 cc. of patient's blood volume) as an anti-fibrinolytic agent.

Moderate systemic hypothermia was used, reducing the rectal temperature to between 28° and 30°C. The esophageal temperature fell to about 25°C. The flow rate was dropped concomitantly with the fall in total systemic temperature as described by Gollan.<sup>7</sup> Prior to the actual valve surgery, the heart was placed in ventricular fibrillation with 60 cycle AC current<sup>8</sup> in the range of 2-4 watts to prevent air embolism and to obtain a motionless operative area.

#### A. Mitral Commissurotomy

After the rectal temperature had dropped to between 28 and 30°C, the left atrium was opened and the mitral valve was closely examined. The fused commissures were sectioned until an adequate opening was obtained. The diameter obtained varied with the size of the valve, ranging from 3 to 4 centimeters.

\* Rheomacrodex, Pharmacia

### B. Mitral Valve Replacement

Once it was determined that the valve should be replaced, the anterior leaflet of the mitral valve was excised, leaving a rim of valve tissue around the mitral ring.<sup>9</sup> The Chordae tendinae attached to the posterior mitral leaflet were left undisturbed. This conserved the downward pull of the papillary muscles<sup>10</sup> on the mitral ring during the early isometric contraction of the left ventricle. The valve was then sutured in place, utilizing 12 to 15 (00) silk interrupted mattress stitches threaded through teflon tubing (4 mm. long) for support and placed circumferentially around the mitral annulus.

The sizes of Starr Edwards prosthesis varied with the diameter of the mitral ring. We used the largest possible size, from a No. 2 to No. 4.

## IV. Results

### A. Mitral Commissurotomy

All patients are alive and have benefited from the procedure. One patient (16 years) has a minimal degree of mitral regurgitation. All except one have a normal sinus rhythm post operatively.

### B. Mitral Valve Replacement

There were six patients in this group, four tolerated the procedure very well and are doing fine. The mortality in this group was 33.3%.

One patient died on the tenth postoperative day secondary to a Pseudomas infection. Post mortem examination of the heart was non contributory. The second death was secondary to an air embolism during the actual replacement of the mitral valve. Inadvertently, the electrical fibrillator became unplugged and the ventricles contracted thus producing air embolism. A trachostomy was performed in the operating room. Post-operatively she was placed on a mechanical respirator. Hypothermia, low molecular weight dextran, steroids, urea, and antibiotics were given. Despite all these energetic measures, she expired on the seventh post-operative day without having regained consciousness. The post mortem findings revealed a bilateral massive broncho pneumonia which is a common precipitating factor in the outcome of this type of patient. The mitral prosthesis was in perfect state.

One patient had a cerebro-vascular accident the third post-operative day and anticoagulant therapy could not be used because

the patient still had the chest tubes. This patient developed a severe infection due to *Pseudomonas auroginosa*. He was placed on "Colymicin", steroids, low molecular weight dextran, hypothermia, and on a respirator. From this episode, he recovered completely and is doing very well. None of the four patients with Mitral Valve prosthesis are on chronic antiprothrombin therapy. Their rythm is normal sinus.

## V. Discussion

We are convinced that very few patients are good candidates for a closed mitral commissurotomy and believe that the treatment of choice for mitral insufficiency is mitral valve replacement. An exception must be made for patients with congenital cleft mitral valve on whom a few simple sutures may correct the regurgitation.

We are very pleased with the commissurotomy that was performed on the three patients who underwent open mitral commissurotomy. They are doing fine thus proving that open mitral commissurotomy is a safer and better procedure than a closed one. All patients with calcific mitral valves, mixed valvular lesion, history of emboli, long standing atrial fibrillation, and old age should undergo an open mitral commissurotomy.

Mitral valve replacement was undertaken on six patients which were severely incapacitated. The four survivors are doing very well. The two deaths were in the post operative period and we believe they were preventable (air embolism and infection).

## VI. Conclusion

- 1) Patients with severely damaged mitral valves can be operated upon successfully and the valve replaced with a ball valve prosthesis. Six cases are reported.
- 2) Three patients underwent an open mitral commissurotomy with excellent results.
- 3) There have been no late complications nor deaths in the follow up period to date (12 months) in any of the patients reported.

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## BUERGER'S SYNDROME

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### Introduction

In 1908, Leo Buerger<sup>1</sup> published a new concept of the pathogenesis of arterial occlusion in pre-senile gangrene. He believed that in some of these patients the initial lesion was a thrombus which gave rise to a reaction in the vessel wall, and he termed this process thromboangiitis obliterans. In 1909,<sup>2</sup> he called attention to the frequent co-existence of migrating thrombophlebitis in these cases. Adding more patients to the original group, in 1914,<sup>3</sup> he emphasized two stages in the pathology of what he was by then referring to as a new disease. The early or acute stage, consisting of a recent thrombus containing miliary foci of inflammatory and giant cells, was specific and probably of infectious etiology. The late stage was characterized by organization of the thrombus and recanalization of the vessel. In addition he described an extensive, diffuse, fibrous thickening about the adventitia of the artery and vein. At times the accompanying nerve was also enveloped by this reaction. During the 1930's and 1940's, the term "Buerger's Disease" found wide acceptance and the diagnosis was frequently made. The clinical criteria, in addition to evidence of arterial insufficiency, and possible concomitant superficial thrombophlebitis, included a relatively recent history of symptoms in young male smokers, usually of the Jewish faith.

During the 1950's, with the popularization of peripheral arteriography, it soon became evident that many cases previously thought to represent Buerger's disease were rather atheromatous obstructions of the femoropopliteal region occurring at an earlier than usual age.

In 1957, in a study of cerebral Buerger's disease, Fisher<sup>4</sup> concluded that the evidence was not sufficiently specific to warrant the concept of a different type of arterial occlusive disease, and that these cases probably represented thrombosis in vessels distal to atherosclerotic occlusion of larger arteries. In 1958, Gore and Burrows<sup>5</sup> published a pathologic study of three cases which

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had been diagnosed by others as Buerger's disease. Postmortem examination failed to reveal any of the changes previously described as characteristic of this disease. In 1960, Wessler et al<sup>6</sup> published an evaluation of occlusive peripheral vascular disease concluding that Buerger's disease is indistinguishable from atherosclerosis, systemic embolism, or peripheral arterial or venous thrombosis. Others (Mc Kusick et al,<sup>7</sup> Horwitz<sup>8</sup>) have defended the concept with equally persuasive data.

We have been interested in Buerger's disease for some time and the present divergence of opinion has prompted us to review our experience with several thoughts in mind. We wanted to know whether the diagnosis of Buerger's disease as we had made it previously could now be substantiated in the light of a closer scrutiny. We also wanted to evaluate the effectiveness of our treatment date and what the course of the disease has been in the years that have elapsed.

### Material and Methods

All the cases previously diagnosed as Buerger's disease at the San Patricio VA Hospital were collected, the records and pathologic material were reviewed and the patients re-examined. The following studies were obtained: complete blood count and hematocrit, urinalysis, serum cholesterol and esters, erythrocyte sedimentation rate, serum transaminase, total protein and albumin-globulin ratio, blood urea nitrogen, serum uric acid, electrocardiography, chest X-ray, and fundoscopic examination. In most cases peripheral arteriography was performed. A total of 26 patients were found with a previous clinical diagnosis of Buerger's disease. Of these, there was amputation material available for study in 18. The histopathologic diagnosis of Buerger's disease was confirmed in 13 of the 18. In the remaining five cases, the changes were not specific enough or pathologic material was inadequate to warrant a definite diagnosis of thromboangiitis obliterans.

The criteria used were as follows: There was thrombotic occlusion of arteries and veins with organization and recanalization. The internal elastic membrane was well preserved as was most of the vessel wall. There was no calcification and minimal, if any, atherosclerosis. The acute lesion was seen in only one amputation specimen, a finger. It consisted of a recent thrombus containing minute microabscesses and giant cells. Amputations were performed relatively late in the course of the disease, and this may account for the relative rarity of acute lesions in our material and that of others.

The 13 patients whose diagnosis was confirmed by histopatho-

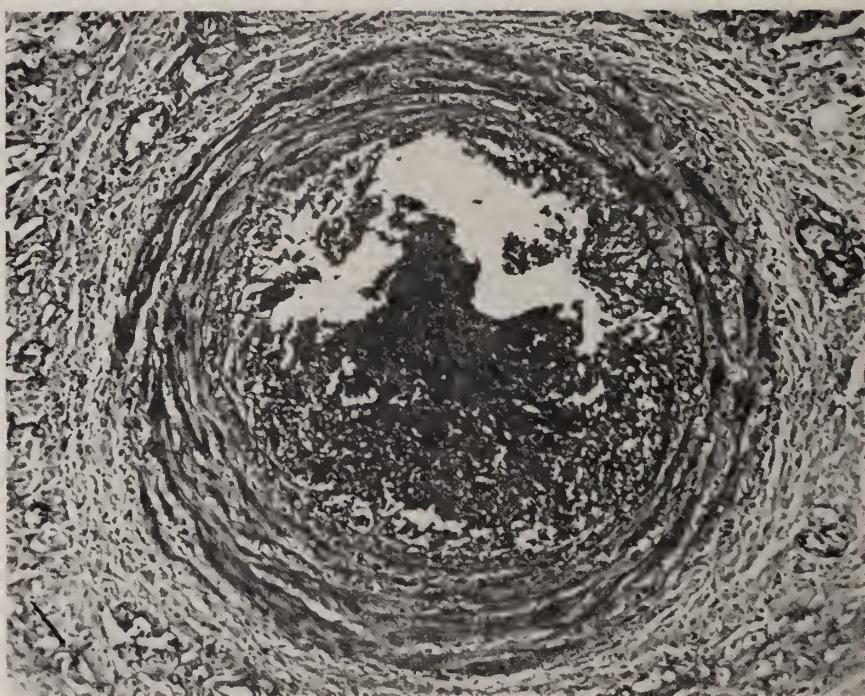


FIG. I. Digital Artery showing thrombosis with microabscesses and Giant cells.

logic study had a mean age of 30 and the oldest was 39 years of age at the time of follow-up examination. Symptoms ranged from five to 12 years in duration. There was arterial insufficiency of varying degree in the involved extremities as evidenced by history of claudication and diminished or absent peripheral arterial pulsations. Ten of 13 had upper extremity lesions as well as in the legs.

Clinically these 13 patients showed three types of lesions. An extremely painful, cold, and purplish finger tip or toe was very often the presenting complaint. They also had either concurrent or previous episodes of subcutaneous inflammatory lesions of the extremities. We found these lesions to consist of either a typical segmental superficial thrombophlebitis or a reddish purple patch of skin and subcutaneous tissue which was extremely painful and very tender to the touch. These patches were oval or round, measured between 1 and 5 cm. in diameter, occurred distally in the arm or leg, and were not found in relation to superficial veins.

The painful nature of these lesions was striking. The usual clinical indexes of infection were absent. There was no fever, leukocytosis, elevated erythrocyte sedimentation rate or alteration of serum transaminases. Most of these patients showed rather high hemoglobin and red blood cell counts, many being over 5 million/cmm. and 15 grams % whereas our usual hospital population

averages 4 million/cmm. and 12 grams %. Indeed, one of the patients rejected from the study was found to have Gaisböck's syndrome, a variant of polycythemia vera. Electrocardiograms and all other laboratory procedures were found to be within normal limits. None of the patients was hypertensive or diabetic and serum cholesterol levels were within normal limits in all.

As regards arteriography, though we have seen some of the features emphasized by McKusick et al,<sup>7</sup> in our hands this study has not been specific enough to establish the diagnosis of Buerger's disease. Rather, it is very valuable in establishing the presence of atherosclerotic femoropopliteal occlusion in young people.

### Treatment

While we have seen dramatic improvement in the acute painful lesions with the use of corticoids, we have also seen it happen following treatment with heparin. It has also happened spontaneously, while the patient was under observation. We are planning to use low molecular weight Dextran in an attempt to improve the microcapillary circulation. If sludging is a factor of importance in the genesis of this disease, low molecular weight Dextran may be of value. So far our attempts in this area have been limited to phlebotomy and no particular beneficial effects have been observed from this procedure. Sympathectomy does result in a warm dry extremity. Many times it does not, or only partially, relieves the pain. It certainly does not prevent progression of the disease. We have often seen further lesions occur in adequately sympathectomized extremities. The administration of estrogens has not proved to be of benefit.

Gore<sup>5</sup> has pointed out that the high incidence of toe and finger lesions suggests a vasospastic factor in the genesis of this disease. In this connection it is interesting to note that even in this tropical setting, where vasospasm due to cold weather is not a significant factor, we have found this very high incidence of toe and finger lesions. The vasospastic effect of smoking on the peripheral arterial tree is well known. The relationship of tobacco to Buerger's disease has been written about for many years and lately is being questioned. All of our patients were heavy smokers and the resumption or continuation of smoking did seem to have a definite deleterious effect on this disease.

The clinical course of our patients has been characterized by exacerbations and remissions. It appears that the disease is in a way self-limited in the patients who stop smoking. Most of them seem to have periods of activity ranging between two and four years. After this time the disease appears to quiet down. Our follow-up in this connection is, admittedly, still much too short.

### Comment

Peripheral arterial insufficiency in young men is caused by atherosclerosis in most cases. However, when in the absence of other evidence of atherosclerosis there are additional findings of cutaneous and phlebitic lesions and a high incidence of finger lesions, these patients warrant a distinct clinical classification, as Horwitz<sup>8</sup> has pointed out.

While the disease may prove to be a variant of atherosclerosis, it is possible that this entity represents some type of collagen disease. Even Leo Buerger's concept of an infectious etiology may yet prove to be correct. We feel it is best to term this process Buerger's Syndrome, as McKusick<sup>7</sup> suggests, until the true nature of this illness is clarified.

### Comentario

La insuficiencia arterial periférica en sujetos jóvenes es causada por la aterosclerosis en la mayoría de los casos. Sin embargo, cuando no existe evidencia de aterosclerosis y en adición tenemos hallazgos de lesiones cutáneas y flebiticas, con una incidencia alta de cambios en los dedos de las manos, estos pacientes requieren una clasificación clínica específica, como ha sugerido Horwitz.<sup>8</sup>

Es posible que esta condición resulte ser una variante de aterosclerosis o que represente algún tipo de enfermedad colágena. Hasta el concepto original de Leo Buerger de que la etiología es infecciosa, puede que resulte ser el correcto.

Creemos que es deseable llamar a este proceso el síndrome de Buerger, como ha sugerido McKusick,<sup>7</sup> hasta que se esclarezca la verdadera naturaleza de esta afección.

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## CONTACT LENSES

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There are millions of contact lenses wearers in the United States of America and also a considerable number of wearers in Puerto Rico. Recently, The Federal Food and Drug Administration released a report by Dr. William Stone, Director of Ophthalmic Plastic Research Laboratories at the Massachusetts Eye and Ear Infirmary, stating, that he has treated 14 cases of blindness or partial blindness associated with wearing plastic lenses. Dr. Stone said that the 14 cases reported since last September were due directly or indirectly to the wearing of plastic contact lenses.

In reviewing the literature I could only find one article<sup>11</sup> that blames loss of vision directly to contact lenses and occurred in two patients following bilateral corneal ulcers with hypopyon due to continued wearing of contact lenses day and night for prolonged time. Personal communications with other ophthalmologists in Puerto Rico have failed to reveal any permanent damage of the cornea in wearers of contact lenses in Puerto Rico. In spite of the fact that there are millions of patients wearing contact lenses of various designs and manufacture, fitted by a variety of techniques, there have been only a very few case reports of eyes lost as direct result of improper wearing or improper handling of contact lenses.

However there have been many reports of transient damage to the cornea.<sup>1,4,5,6,7,10,11,13</sup> It is stated that about 1% of contact lenses wearers develop pathological changes in the cornea. A contact lens is a prosthesis and like other prosthetic devices it causes anatomic and physiologic changes in the tissue it approximates. Anatomically, the shape of the cornea may be altered, resulting in a change of the radius of curvature. Physiologically, the carbohydrate (glycogen) and ribonucleic acid metabolism are altered to more nearly anaerobic conditions. Corneal parasthesias and thickening also result.<sup>1,5</sup>

Fonda<sup>13</sup> classifies early complications as initial foreign body reaction such as blepharospasm, lacrimation and photophobia, which lasts for five to ten minutes, the contact lens may be dislodged at this stage, and early adaptation complications such as epithelial edema with punctate staining may occur. Late complications are continuing corneal edema demanding less wearing time, corneal scratching on insertion, apical erosion of the cornea due to a lens with too flat a posterior curve, trapping of foreign body

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under the lens, infected corneal abrasion and corneal strangulation. The latter complication occurs usually due to a lens with a posterior curve that is too sharp and the lens becomes adherent to the peripheral flatter portion of the cornea, more like a suction cup. This prevents metabolic exchange of oxygen, carbon dioxide, hypertonic tears, and heat by tear evaporation between the environments on either side of the contact lens. Corneal epithelium and stroma become edematous and the epithelium may show superficial changes. Fortunately, these late complications produce reversible corneal changes when not infected and improve rapidly by patching the affected eye with antibiotic ointment for about 24 hours. However, the prolonged use of improper contact lenses or the prolonged use of proper contact lenses without intermittent periods of rest or under poor hygienic conditions, have been the cause of blindness of very few wearers. It has been proven in experimental rabbits' cornea that under those conditions there is vascularization and ulceration of the cornea,<sup>6</sup> and when treatment has not been instituted promptly irreversible damage to the cornea occurs.

At this stage we can resume that the pathologic complication which is most feared is infection. Early and adequate therapy should control it. Diabetics, people on heavy steroid medication, aged or debilitated patients, and people with poor working conditions or with infections and allergies of the lid, conjunctiva, and cornea should be considered as greater pathologic risks.<sup>5,13</sup>

Even though cosmetic reasons are the main demand for contact lenses, particularly in myopes, more medical indications have been gradually found for them. Nowadays, beside their general use in monocular aphakia, keratoconus and irregular astigmatism, they have been useful in diseases, injuries, and neoplasms of the lids and conjunctiva, irritative lesions of the cornea, such as vernal catarrah, paralytic ptosis associated with facial paralysis,<sup>14</sup> aphakia in infants,<sup>3</sup> cornea plana, plastic surgery of the eyes, and in certain errors of refraction to give binocular vision to the patient when there is considerable degree of anisometropia or aniseikonia, aside from monocular aphakia, and to improve the vision in high myopes. In the latter, vision is much better with contact lenses than with spectacles.

They are useful too for the cosmetic correction of corneal opacities; for stage, screen and television personnel, athletes, truck drivers, sailors, and surgeons to prevent fogging of spectacles.

Not all patients are able to wear a contact lens. According to Girard<sup>7</sup> this might be for a number of reasons, such as:

1. The presence of corneal pathology.

2. Lacrimal insufficiency. This is particularly true in the older age group in which some degree of lacrimal insufficiency is common.
3. Subjective complaints. There is a certain amount of physical discomfort wearing a contact lens, even though this has been minimized by recent designs and fitting techniques. Some patients have been so bothered by the physical awareness of the contact lens, that they are unable to wear it. Cochet<sup>4</sup> believes that there are some patients that have a fragile corneal epithelium prone to develop corneal abrasion. He has termed it "epithelial fragility". This is determined by pressing on a contact lens with a tonometer for four minutes and noting with the biomicroscope the degree of corneal abrasion that results.
4. The lack of manual dexterity in removing and inserting a contact lens.
5. Psychological block against contact lenses. There are some patients, even those with great motivation, who develop a "mental block" against contact lenses and are unable to wear them.

In conclusion, let me say, that contact lenses are now a major part in the correction of visual errors. Not only are they practical in many diseased conditions, but they are very practical for people who are taking part in sports, as well as helping those people who have an inferiority complex.

Ophthalmologists must accept their responsibility. There are many persons that are being fitted with contact lenses that should have been screened and should not be wearing contact lenses. Every case should be examined to make certain that there are no contraindications to the use of wearing contact lenses.

Therefore the responsibility belongs to the physician and every attempt should be made by the young ophthalmologist to learn everything he can about fitting contact lenses.

The dispensing of spectacle lenses has, traditionally, been relegated to opticians. This may explain the reluctance of the ophthalmologists to personally fit or closely supervise the application of contact lenses. Vanzant calls attention to the AMA resolution that fitting contact lenses is a medical act.

Since 1962 I have fitted more than 50 contact lenses. Formerly, I was very reluctant to interfere with the application of contact lenses, but since 1963 every day that goes by I am more satisfied with fitting them and I am convinced that the armamentarium of the ophthalmologist is not complete until he fulfills

his medical duty to engage in the fitting or the close supervision of the application of contact lenses.

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## CONGENITAL ANOMALIES OF THE EXTERNAL GENITALIA

BERNARDINO GONZALEZ-FLORES, M.D.\*

This study presents the congenital anomalies of the external genitalia observed in 5461 consecutive deliveries during a period of 13 months at the San Juan City Hospital, San Juan, Puerto Rico. All the anomalies encountered were limited to the male sex. The total males examined were 2788 of which 295 were prematures. A good follow up for at least a period of 2 years was obtained in 85 percent of the hydroceles and about 50 percent of the cryptorchids. The posterior urethra, bladder, and upper urinary tracts were not investigated. Congenital phimosis was not included in this study because it is present in about 100% of newborns and therefore I consider it a physiological condition.

Table 1 lists the anomalies observed in order of frequency. The incidence of congenital anomalies of the external genitalia in the male amounted to 2.04 percent.

### CRYPTORCHIDISM

In table II incidence of the most common anomalies is presented. The incidence of cryptorchidism among premature infants (4.74%) was over four times higher than the incidence of the same condition in the full term babies (1.12%).

A breakdown of the cases with cryptorchidism is shown in table III. Cryptorchidism was more frequently observed in the right than on the leftside. Unilateral cryptorchidism predominated among the full term newborns while bilateral undescended testes was more commonly encountered in the premature infants.

Table IV illustrates the follow-up in 20 cases of cryptorchidism secured during their first two years of life. The testes descended to the scrotum during the first year in eleven cases (55 per cent), the other nine cases (45 per cent) failed to descend by the end of the second year of age.

It is interesting to note that in the four premature infants followed with bilateral cryptorchidism the testes descended to the scrotum in all instances during the first year of life. The same was observed in three out of four bilateral full term cryptorchids. However, only about a third of the unilateral undescended testes reached the scrotum by the end of the second year of life.

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TABLE I  
ANOMALIES OF EXTERNAL GENITALIA IN 2788  
NEWBORN MALES

CRYPTORCHIDISM -----	42
CONGENITAL HYDROCELE -----	12
HYPOSPIADIAS -----	8
ABSENT FRENULUM -----	2
PENILE RAPHE DEVIATED AWAY FROM MIDLINE WITH DEVIATION OF PENIS -----	2
PENIS BURIED IN SCROTUM -----	1
TORSION OF SPERMATIC CORD -----	1

TABLE II  
INCIDENCE IN 2788 NEWBORN MALES

	No. of Cases	Incidence
CRYPTORCHIDISM -----	42	1.51%
TERM -----	28	-----
PREMATURE (295) -----	14	-----
HYDROCELE -----	12	0.43%
HYPOSPIADIAS -----	8	0.28%

TABLE III  
CRYPTORCHIDISM IN 2788 NEWBORN MALES

	No. of Cases	Term	Premature
BILATERAL	20	9	11
RIGHT	14	11	3
LEFT	8	8	0
TOTAL	42	28	14

TABLE V  
CRYPTORCHIDISM, FOLLOW-UP OF TESTES  
WHICH DESCENDED TO SCROTUM

No. of cases	Term	Premature	Total Term and
			Premature
Bilateral	8	3 (75%)	4 (100%)
Unilateral	12	4 (33%)	7 (87.5%)
		Total	11 (55%)

## CONGENITAL HYDROCELE

In order to avoid confusion in the terminology,<sup>3</sup> I wish to emphasize that in this study term congenital hydrocele applies to those hydroceles of the cord or hydroceles of the testis encountered at the time of birth and in which there is no communication between the cavity of the tunica vaginalis and the peritoneal cavity (patent processus funicularis). An accumulation of fluid in the cavity of the tunica vaginalis because of a patent processus funicularis is not a hydrocele but rather a congenital indirect inguinal hernia.

Hydrocele was encountered in 12 instances among 2788 consecutive male infants, which amounted to an incidence of 0.43%. Seven were bilateral, four in the right and one in the left side. Hydroceles were not observed among prematures. All hydroceles were diagnosed as hydroceles of the testis at the time of examination. No hydrocele of the cord among the males and no hydrocele of the canal of Nuck in over 3,000 female newborns examined were found.

Follow-up was obtained in 10 infants with hydrocele. It was not a surprise to find out that in 9 cases the hydrocele disappeared before the first year of life, the majority during the first few months after delivery.

In the tenth infant in whom a diagnosis of hydrocele of the testis was made on the day of delivery, a herniorrhaphy for a congenital indirect inguinal hernia was performed at the age of two years. In retrospect, it is obvious that this infant had a very small communication between the cavity of the tunica vaginalis and the peritoneal cavity which resulted in an accumulation of peritoneal fluid within the tunica vaginalis. The reason why this particular "hydrocele" did not disappear was simply because it was not a hydrocele, it was a congenital indirect inguinal hernia.

## HYPOSPADIAS

Only eight cases of hypospadias with an incidence of 0.28 per cent were observed. Six infants had glandular hypospadias, one penile and one peno-scrotal. Hypospadias was not observed among the female or prematures. The external urethral meatus was narrowed in most of the cases of hypospadias and a bifid scrotum accompanied the only case of peno-scrotal hypospadias.

## DISCUSSION

An analysis of the data presented in this study brings about several interesting observations.

### 1. The Descent of the Right Testis as Compared to the Left.

This study and a review of the literature<sup>6,7</sup> showed that cryptorchidism is more frequently observed in the right than in the left side. Similarly, a greater frequency of congenital indirect inguinal hernia has been found in the right side. The preponderance of right sided undescended testes and congenital indirect inguinal hernias is probably related to a delayed descent of the right testis as compared to the left. Among the unilaterally premature cryptorchids in this report, three were encountered in the right side and none in the left. Although this is a very small series of cases, it shows a preponderance of right undescended testes among the prematures which gives support to the belief that the right testis descends at a somewhat later date than the left.

### 2. The Time of Descent of the Testis to the Scrotum.

Several investigators<sup>2,3,8</sup> claim that the descent occurs during the latter months of pregnancy ranging from the 7th to the 9th months. In this study in which 2493 consecutive fullterm newborn males were examined, the testes had descended to the scrotum at the time of delivery in 98.9% of the cases. In the 295 consecutive premature male newborns examined, the testes had reached the scrotum at the time of delivery (7th to 8th month) in 95.3% of the cases. If, according to the presented data, over 95% of the premature newborns have the testes in the scrotum between the 7th and 8th month of gestation, it is a logical deduction that the testes descend to the scrotum prior to the 7th month and not during the latter months of gestation, as is generally accepted.

The role of maternal gonadotrophin<sup>2,4</sup> in the descent of the testes has been well established by Engle<sup>5,6</sup> who precipitated the descent of the testes in ten immature macacus monkey following injection of extracts of pregnancy urine. The peak of maternal gonadotrophin during gestation occurs between the fifty-second and sixty fifth day with a sharp decline after the sixty seventh day. After the 120th day, a relatively low and constant level is reached and maintained until delivery. Following delivery, the chorionic gonadotrophin normally disappears from the blood and urine within three to ten days. If the maternal gonadotrophins participate in the descent of the testes to the scrotum and their maximum stimulus is observed during the third month of gestation, the testes may descend to the scrotum at the third or fourth month of pregnancy. There is a great need for investigation of the testicular descent in stillbirths, fetuses, and prematures, as well as the effect of the chorionic gonadotrophin hormone in the fetal testis.

### 3. The Time of Descent of Undescended Testes.

The majority of bilateral undescended testes descended to the

scrotum during the first year of life. However, only about a third of the unilateral undescended testes reached the scrotum at the end of the second year of life.

#### 4. The Mechanism Which Explains the Formation of Congenital Hydroceles and Its Disappearance During the First Few Months of Life.

According to Allen, Lane & Rinker, J.R.,<sup>1</sup> the lymphatics of the tunica vaginalis develop late and, if the communication between the tunica vaginalis and the peritoneal cavity closes before the lymphatics are completely developed the child will have a congenital hydrocele. The reason why infants with congenital hydrocele usually recover spontaneously is because the lymphatics go on to develop after birth. I do not agree with the above theory, first, because it is hard to imagine a selective underdevelopment of the lymphatics of the tunica vaginalis and spermatic cord while in other parts of the body the lymphatics are normal. In the second place, if the lymphatics are not completely developed at the time of birth of the fullterm infant, then it is logical to assume that they are less developed in the newborn premature. Therefore, the incidence of hydroceles among the prematures would be expected to be higher than in the fullterm babies. However, this is not supported by evidence in the analysis of the congenital anomalies presented in which no hydroceles were observed among the premature infants.

In the normal cavity of the tunica vaginalis there is a continuous but slow interchange of fluid which maintains a constant volume as long as there is a balance between production and reabsorption. Certain conditions such as infection and trauma result in an increased production of fluid while lymphatic obstruction is responsible for decreased reabsorption. The balance between production and re-absorption is disrupted resulting in the formation of a hydrocele. As soon as the irritation or obstructing factor is eliminated, increased re-absorption of the accumulated fluid occurs with the eventual disappearance of the hydrocele. In the newborn, another mechanism responsible for the formation of a congenital hydrocele is a trapping of peritoneal fluid within the cavity of the tunica vaginalis at the time of closure of the processus funicularis.

#### 5. Congenital Hydrocele Versus Congenital Hernia.

Congenital hydroceles usually disappear spontaneously during the first year of life. The congenital indirect inguinal hernia should be suspected among infants with a persistent accumulation of fluid in the tunica vaginalis. In these cases there is a patent processus funicularis with a very small communication between the peritoneal cavity and the cavity of the tunica vaginalis which

permit only the passage of peritoneal fluid. If the communication between the two cavities becomes wider, abdominal viscera will also descend resulting in a classical indirect inguinal hernia.

There is a way to differentiate the congenital hydrocele (hydrocele present at time of birth) from an indirect inguinal hernia with only fluid accumulation in the hernial sac. In the recumbent position, if the fluid within the tunica vaginalis is forced into the peritoneal cavity by scrotal manipulation, the condition is an inguinal hernia, otherwise, it is a congenital hydrocele.

#### SUMMARY

An analysis and follow-up of the congenital anomalies of the external genitalia encountered among 5461 consecutive deliveries is presented. The most common anomaly observed was cryptorchidism followed by congenital hydrocele and hypospadias.

The majority of bilateral undescended testes descended to the scrotum during the first year of life while only a third of the unilateral undescended testes descended by the end of the second year.

All' congenital hydroceles disappeared spontaneously during the first year of life. The mechanism involved in the formation and disappearance of congenital hydrocele and the relationship between congenital hydrocele and indirect inguinal hernia are discussed.

#### RESUMEN

Este estudio representa un análisis de las anomalías congénitas de los órganos genitales externos encontrados en 5461 nacimientos consecutivos.

La anomalía más comúnmente encontrada lo constituyó el criptorquidismo seguido por hidroceles congénito e hipospadias.

Se pudo comprobar que en la mayoría de los casos con criptorquidia bilateral el descenso de los testículos tuvo lugar durante el primer año de vida, mientras que en los casos de criptorquidismo unilateral solamente en la tercera parte se produjo el descenso del testículo al finalizar el segundo año de vida.

Todos los hidroceles congénitos desaparecieron durante el primer año de vida. El mecanismo envuelto en la formación y desaparición del hidroceles congénito y su relación con la hernia inguinal indirecta ha sido objeto de discusión en este trabajo.

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## "PAIN IN THE UPPER EXTREMITY"

NATHAN RIFKINSON, M.D.

Whenever a number of possible causes tend to produce a group of similar symptoms, there is a tendency to apply the term syndromes, such as shoulder arm syndromes or thoracic outlet syndromes. The gross effect of these designations on our thinking is to discourage us from tackling the job of unraveling their complex ramifications, and the patient who suffers from one of these syndromes is subjected to long delays and nebulous therapeutic trials.

But if we should consider pain in the upper extremity by itself, we are more likely to arrive at its cause simple considerations.

Pressure against a nerve will produce pain, and the most likely place in which pressure can occur is the region of greatest anatomical crowding. It is for this reason that most discomfort in the upper extremity can be traced to some abnormality at the base of the neck.

Just behind the clavicle the anterior and medial scalenii muscles are attached to the first rib a few centimeters apart. Through this small space between these two muscles, and resting on the upper surface of the first rib as they run into the axilla, are the components of the brachial plexus, and lying snugly anterior to and against the lower trunk of the brachial plexus, and behind and touching the anterior scalenus muscle, is the second portion of the subclavian artery. Thus, we have several sensitive structures situated between two muscles in the most movable and most vulnerable region of our body. Thus, anything that will crowd this small space, a tumor, a cervical rib, a thick or spastic scalenus muscle, may cause pressure against the artery or nerves or both.

Today I wish to dwell only on the most common of the causes of pain in the upper extremity for which a great deal can be done, but which, for several reasons, is neglected more than it should be and, at times, is grossly disregarded. I refer to the pressure of the anterior scalenus muscle against the subclavian artery with secondary pressure by the artery against the components of the brachial plexus, or the scalenus anticus syndrome.

This syndrome, which has been known for many years, has been very elusive, first, because of its sheer simplicity; second, because of the immediate mental assignation by the physician of

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upper extremity pain as part of the complicated shoulder arm syndromes giving a defeatist attitude to start with; and, third, because of the dependence on, and the misinterpretation of, the various tests used.

I wish to liberalize the diagnostic criteria for this syndrome, because it is often unjustly eliminated as the etiology of pain in the upper extremity because one or another factor of certain tests is missing.

The absence of a cervical rib does not eliminate the scalenus anticus syndrome, neither does the absence of a reduced pulse on certain maneuvers. Yet, if one or the other of these criteria is absent, there is a tendency by many of us to eliminate it.

There are several tests which are used indiscriminately and frequently wrongly to determine the presence of the scalenus anticus syndrome. One is to feel the patient's pulse with the arm extended and mildly abducted, and the shoulders pulled down and backward, similar to someone standing at attention. This ap-



FIGURE I  
Costo-clavicular syndrome.



FIGURE II  
Pectoralis minor or humeral head syndrome.

proximates the clavicle with its subclavius muscle to the first rib and may compress the nerves and vessels in the narrowed costoclavicular space, reducing the arterial pulse and may also increase and produce pain—(Figure I). This does not mean that the scalenus anticus is at fault, but rather that the position of the clavicle is abnormal, as in a poorly approximated fracture, or that the subclavius muscle is hypertrophied. Sectioning the scalenus muscle will bring no relief. Decreased pulse with this maneuver may be present in normal people.

Another test used is abducting the arm above the head. This maneuver tenses the pectoralis minor tendon which may compress the artery and the nerves, reduce the pulse, and produce pain. The head of the humerus may also exert pressure—(Figure II). Some people who sleep with arms above their heads, or who have to work with their arms above their heads, may develop this type of pain in the upper extremities. In such cases scalenus section

also fails to relieve pressure. The only test that will narrow the subclavian space and determine scalenus crowding is done by feeling the patient's pulse with arm extended, ear turned to the same side, and the patient taking a deep breath and holding it—(Figure III). This may reduce the pulse rate in some cases where the scalenus anticus is involved. But if the pulse rate is not reduced, this does not eliminate a scalenus anticus syndrome.

The usual patient with scalenus anticus syndrome complains of a diffuse discomfort in the arm and forearm and weakness of his hand, while the patient with root pressure, due to a cervical disc, can actually trace a line from the back of his neck to the base of one or two fingers, this being a monoradicicular syndrome. The nebulous localization of pain in the scalenus anticus patient is caused by a polyradicular syndrome, pressure being exerted

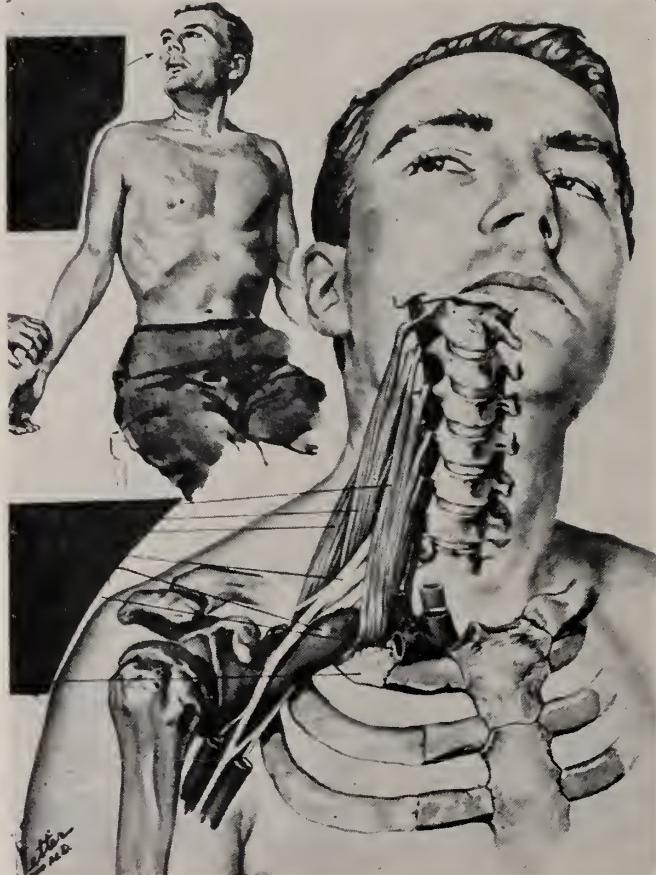


FIGURE III  
Adson Maneuver.

Figures I, III, and II from Clinical Symposia (Ciba) Vol. 10 #2 - March-April 1958.

against a trunk which is a combination of several roots. Since the subclavian artery lies against the lower trunk of the brachial plexus which is composed of the C8 and T1 roots, the patient with scalenus anticus syndrome usually feels numbness or tingling in the fourth and fifth fingers. At this point, special tests are not necessary. These patients tenderness at the insertion of the scalenus muscle, and mild pressure at this site may increase their symptoms.

However, the surest and simplest method is to inject 1-1/2 to 2 cc of 2% procaine directly into the muscle — (Figure IV and Figure V). If correctly done, the spastic muscle will relax and reduce pressure against the artery, which in turn releases pressure against the lower trunk. A positive test will work in from one to several minutes. The strength in the grip increases, the hypesthesia decreases or disappears, and the pain is greatly or completely relieved. However, if the pain disappears but the hypesthesia increases, and the grip becomes weaker, then the test is unsatisfactory because the needle has penetrated to the other side of the muscle and has spilled novocaine onto the brachial plexus. If the pain disappears, and the grip gets better, and a Horner's is produced, then this also indicates that the test is unsatisfactory, since in this instance the stellate ganglion has been anesthetized.

Relief from a successful scalenus muscle injection may last for several minutes to several hours. Four out of five patients

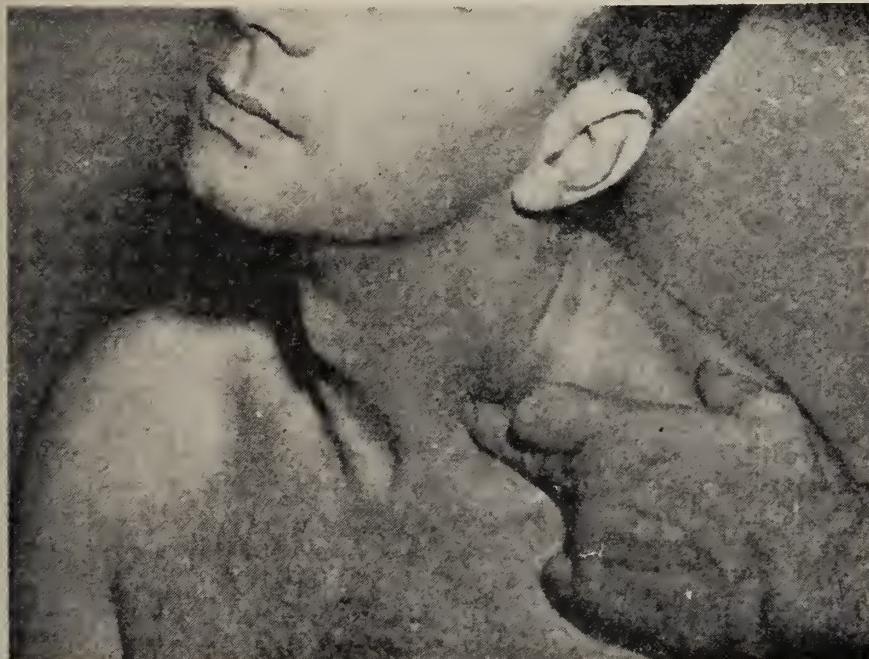


FIGURE IV



FIGURE V  
Method for locating scalenus anticus muscle.

Figures IV and V from pages 104 and 105. Segmental Neuralgia in Painful Syndromes - Judovich & Bates 1946.

will experience permanent relief from their symptoms after four to five injections, the procaine having finally broken the cycle of scalenus muscle spasm. If the duration of the relief is for only a few hours or less, but returns after four to five scalenus injections, then scalenotomy is indicated.

Because the subclavian artery has sympathetic fibers, scalenus anticus compression may irritate these fibers causing reflexly duskeness and puffiness of the hand, and even ulceration of the tips of the fourth and fifth fingers. Of course the other fingers may be involved altho rarely, if the upper components of the brachial plexus are compressed between the scalenus anticus and medius muscles.

When operating on these patients it is best to be very careful in separating the anterior scalenus muscle from the subclavian artery just behind it before sectioning the muscle as close to the rib as possible, because in long standing cases there may be atherosomatous changes in the arterial wall and adherence to the muscle posteriorly, and as the muscle retracts upward as it is sectioned, it may tear a hole in the artery. After successfully sectioning the muscle, the artery must then be dissected off the brachial plexus,

and, if properly done, will move inferiorly. Unless this is done, the patient will no always experience relief.

The most common cause of initiating pain in the upper extremity is either chronic or acute downward pulling of the shoulder, as in lifting heavy suitcases, ironing for long periods of time, or similar strenuous movements. However, I wish to emphasize another common cause, which, by its very nature, tends to confuse the clinical picture. We have noticed that many patients, after recovering from minor or major head injuries, later complain of pain in one or both arms. Because the force of the blow to the head is propelled downward, there may be indirect injury to the cervical spine; or a blow to the side of the head may cause a sudden lateral displacement and stretching of the neck muscles. Our attention is naturally directed to the cervical intervertebral discs. And if one or more of the cervical interspaces are found on x-ray to be narrowed, our suspicions are riveted onto the discs.

I have in mind a forty-three year old man with a history of head injury who later complained of pain and weakness in the left upper extremity for several months. When, after extensive physiotherapy and head traction, he failed to respond, a myelogram was performed and a defect found at C7-T1 level on the left (Figure VI). The patient was scheduled for laminectomy, but then transferred to the San Patricio Veterans Hospital here. On examination the patient was found to have a tender left scalenus muscle and some interosseous atrophy. Novocaine injections relieved the pain temporarily, and in surgery the scalenus muscle was found hypertrophic and the subclavian artery compressed. It is quite probable that a number of patients undergo cervical disc surgery when the cause is the scalenus muscle.

The same situation is at times encountered in direct cervical or whiplash injuries.

A sixty-four year old worker fell ten feet onto the back of his head and dislocated C6 on 67 with resultant quadriplegia. After several weeks in crutchfield tongs, and several months in a four-poster collar, the patient recovered practically normal movement. But he had been complaining of pain and weakness in both upper extremities. The C5-C6 and C6-C7 disc spaces were very narrow and at first bilateral rupture of the cervical disc at C6-C7 interspace was suspected. But since the patient had bilateral scalenus anticus tenderness, these muscles were injected with novocaine several times with temporary relief. Bilateral scalenus anticus section eliminated the patient's pain.

In another instance a forty-three year old housewife who had suffered pain and swelling of the right upper extremity for several months, developed ulceration of the tips of the fourth and fifth



FIGURE VI

Cervical myelogram showing defect at C7-T1 level, left.

fingers. She was scheduled for upper thoracic sympathectomy. But, here too, the novocaine test relieved the patient's pain and scalenotomy made the more extensive upper thoracic sympathectomy unnecessary.

In twenty-three carefully selected cases in which the scalenus anticus muscle was cut, two failed to get relief. One, a nineteen year old woman had just married and was going on her honeymoon, when she developed severe pain in the right upper extremity while lifting a heavy valise onto the scale at the airport. At surgery, the subclavian artery at the site of contact with the scalenus muscle, was narrowed to approximately two thirds of the normal, and although it was separated from the lower cord, the artery did not change its position or caliber. Here, a sympathectomy most probably would have helped, but the patient refused. The second case was a twenty-six year old albino woman who had experienced pain in the left upper extremity for two years. A

servical rib was present. When the procedure was explained to the patient, she wanted only her muscle cut. After muscle section, the artery was freed from the plexus and the nerves seemed fairly loose on the cervical rib. But the relief which the patient obtained was not complete.

The question frequently arises: Is there any particular danger to the patient if scalenotomy is not done?

Aside from the discomfort which the patient constantly experiences, and its effects on general living, there is the added possibility of atheromatous change in the artery which can lead to thrombosis. If there are reflex vascular changes as a result of scalenus pressure, long delay can produce not only trophic changes in the joints of the fingers but frank gangrene of the digits. In these cases surgery is mandatory before these changes become permanent.

#### SUMMARY

Pain in the upper extremity is usually caused by chronic or acute irritation of the scalenus anticus muscle. Several simple criteria for determining the presence of scalenus anticus syndrome are discussed, along with indications for surgery. Twenty-three selected surgical cases are discussed with the results of scalenus anticus section.

#### RESUMEN

El dolor en la extremidad superior es frecuentemente causado por irritación crónica o aguda del músculo escaleno anterior. En este artículo se presentan los criterios y las maniobras clínicas que se usan para diagnosticar el síndrome del escaleno anterior. Se discuten las indicaciones para cirugía. Se presenta además una discusión de 23 casos seleccionados en los cuales se hizo cirugía.

**HIATAL HERNIA AND PEPTIC ESOPHAGITIS**

Hiatal hernia occurs in about one third of the population past the age of 40 and its presence is usually demonstrated at the time of an upper gastrointestinal roentgenogram. The existence of a hiatal hernia is of no clinical significance, in the vast majority of the patients, and it is only when it results in the development of peptic esophagitis that the clinician is called upon. Why do some hiatal hernias produce peptic esophagitis? Only when the herniation results in the destruction of the closing mechanism of the esophagogastric junction will esophagitis develop. Radiography usually reveals the regurgitation of the barium meal in the supine or Trendelenburg position or by Valsava's maneuver. Digestion of the esophageal lining results in the classical symptomatology of retrosternal pain, acid eructations, regurgitation of acid chyme, bleeding overt or occult, progressive obstruction to passage of food, and occasionally perforation of the esophagus. The symptomatology is aggravated by posture since the erect position often prevents massive regurgitation.

What can the physician do for this patient? The causative factor of reflux into the esophagus is a mechanical disturbance of the esophagogastric junction and the medical management is directed at neutralization of gastric secret. Since the problem is a mechanical one, neutralization, to be effective, must be carried out throughout the 24 hours and the patient must be maintained in a position that prevents reflux. Thus it is obvious that this management can only be reserved for the mildest forms of esophagitis. Certainly it can not be curative and symptoms return if the treatment is not continuously and carefully carried out.

In the past, surgical treatment was reserved for the most recalcitrant and difficult cases usually those having serious complications. Modern surgery deals with this mechanical problem quite efficiently and with a minimal morbidity and mortality. In fact, the mortality rate is the same as that obtained following cholecystectomy, or an exploratory laparotomy and lower than the mortality for peptic ulcer surgery. Technically the maneuver is usually performed through an abdominal route and consists in the restoration of the closing mechanism of the esophagogastric junction. Other procedures such as vagotomy and pyloroplasty; fixation to the abdominal wall and/or diaphragm are sometimes added to the repair, but its advantages have as yet to be proven. The hiatal de-

fect may be closed in cases of herniation, but the value of this manuever can not be ascertained.

In summary, it is our feeling that esophageal reflux is the cause of peptic esophagitis and that it may or may not be associated with herniation through the esophageal hiatus. Esophagitis is the result of mechanical failure of the closing mechanism of the esophagogastric junction and that a cure of the disease can be safely accomplished in the great majority of instances by a surgical procedure addressed to this goal.

**F. L. Raffuci, M.D.**  
Professor of Surgery and  
Head of the Department  
University of Puerto Rico

## PRINCIPLES OF MEDICAL ETHICS

### P R E A M B L E

#### 4. Clinic

The Principles of Medical Ethics are themselves the criteria by which the ethical nature of professional conduct is determined. In connection with any definition of the word "clinic," it should be clear that regardless of how clinic is defined each physician-member of the clinic must act, in his relations with his patients and his colleagues, in accord with all the Principles of Medical Ethics. No physician member of a clinic may permit the clinic to do that which he may not do. Each physician must observe all the Principles of Medical Ethics.

Under the ethical principles of medicine no use may properly be made of the word clinic that would mislead or deceive the public, or would tend to be a solicitation of patients to the particular group of physicians holding themselves out as a "clinic." **(Judicial Council 1957)**

#### 5. Groups and Clinics

The ethical principles actuating and governing a group or clinic are exactly the same as those applicable to the individual. As a group or clinic is composed of individual physicians, each of whom, whether employer, employee or partner, is subject to the principles of ethics herein elaborated, the uniting into a business or professional organization does not relieve them either individually or as a group from the obligation they assume when entering the profession. **(Principles of Medical Ethics, 1955 edition, Chapter I, Section 3)**

#### 6. Pharmacists

Physicians should recognize and promote the practice of pharmacy as a profession and should recognize the cooperation of the pharmacist in education of the public concerning the practice of ethical and scientific medicine. **(Principles of Medical Ethics, 1955 edition, Chapter VIII, Section 3)**



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## THE PROPERTIES OF OLIVE OIL

by Dr. F. María Segovia de Arana

"Thus, olive oil is unique among vegetable oils by reason of its organoleptic characteristics. Its natural aroma and taste are regarded pleasant by the consuming public in all countries. It need not be refined; it is the only oil that can be consumed in the West in its natural state. This is most important, because in the course of refinement, oils are to some extent transformed and lose some of their nutritive properties."

### COMPOSITION AND CHEMICAL PROPERTIES OF OLIVE OIL

"In the charte below, taken from Hilditch (The chemical constitution of natural fats) the composition in saturated fatty acids (miristic, palmitic and stearic and non saturated (oleic and linoleic) of olive oil in various countries is shown.

#### OILS.

	Miristic	Palmitic	Stearic	Oleic	Linoleic
Italy (Tuscany)	1,1	9,7	1,0	79,8	7,5
Córcica	1,1	9,4	2,0	84,5	4,0
California	1,1	7,0	2,3	85,8	4,7
Spain	0,2	9,7	1,4	81,6	7,0
Tunis	1,1	14,7	2,4	70,3	12,2
Palestine	0,5	10,0	3,3	77,5	8,9
Greece (Rhodes)	0,4	19,7	0,3	69,6	10,4

As can be seen, olive oil, apart from containing a large proportion of a non saturated fatty acid, of twofold linkage, namely oleic acid, also contains lesser quantities of others that have more than a twofold linkage."

## PHITOSTERINES

"Olive oil contain "phitosterine", which, as its name indicates consists of vegetable sterines similar to the colesterine of animal fats, but with the interesting biological characteristic that they are not absorbed by the wall of the stomach and what is even more important, that they prevent, to a greater or lesser extent, the intestinal absorption of the colesterine contained in food, as has been recently demonstrated by the experiments carried out by the Chaikoff School in the United States."

## ARTERIOSCLEROSIS AND OLIVE OIL

"The experiments carried out by Dr. Bronte Stewart in South Africa, demonstrated that colessterol in the blood increased when the subjects consumed animal fats, but this did not occur with vegetable fats, such as sunflower oil, olive oil, etc.

The same type of result was achieved by a group of investigators (among others, Dr. P. D. White, President Eisenhower's personal physician, and Dr. Keys) in a test carried out in Calabria and Crete on subjects whose ages varied between 45 and 65 years and the fatty part of whose food consisted almost entirely of oil. Only two out of the 657 persons examined were seen to have had heart attacks. When this group was compared with a similar one, as regards age, in the United States, whose diet largely included large quantities of animal fats, sixty cases of heart attacks were discovered.

("Time" magazine, 30 December 1957)."

## CONCLUSIONS OF THE WORK OF DR. SEGOVIA DE ARANA

"We must be careful and only recommend such things as can reasonably be expected to do more good than harm. In our opinion, the following measures are reasonable and well founded:

- 1) Reduce the total consumption of calories and in particular those derived from fats, to the amounts consumed, (and which quantities should be maintained) when the body weight is normal between twenty one and twenty five years of age. It is advisable to use non saturated vegetable oils in lieu of animal fats.
- 2) Take active daily physical exercise.
- 3) Avoid all excess (tobacco, alcohol, emotional tension) but such habits need not be cut down drastically.
- 4) Treat arterial hypertension if it appears."

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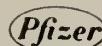
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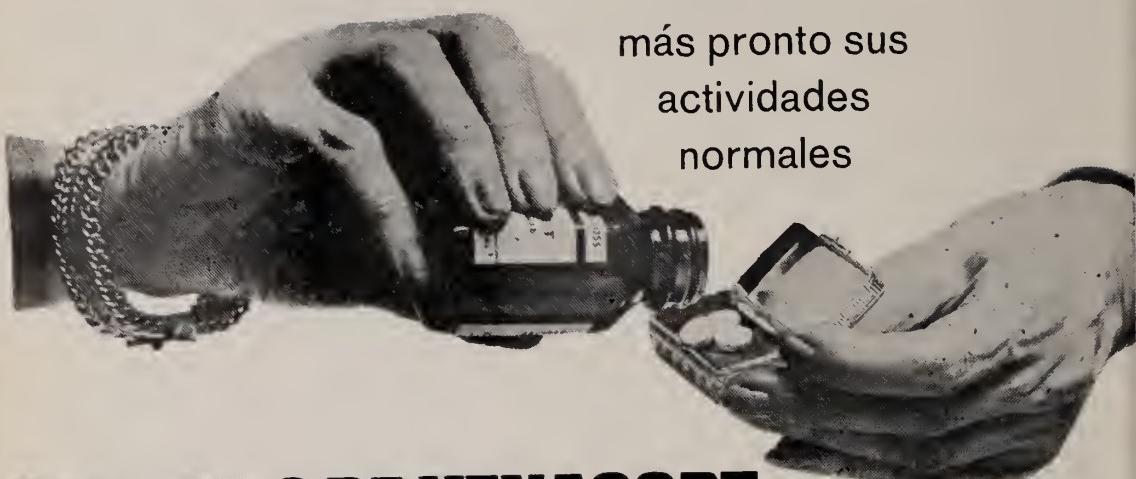
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g) Deben usarse los nombres genéricos de los medicamentos. Pueden usarse también los nombres comerciales, entre paréntesis, si así se desea.

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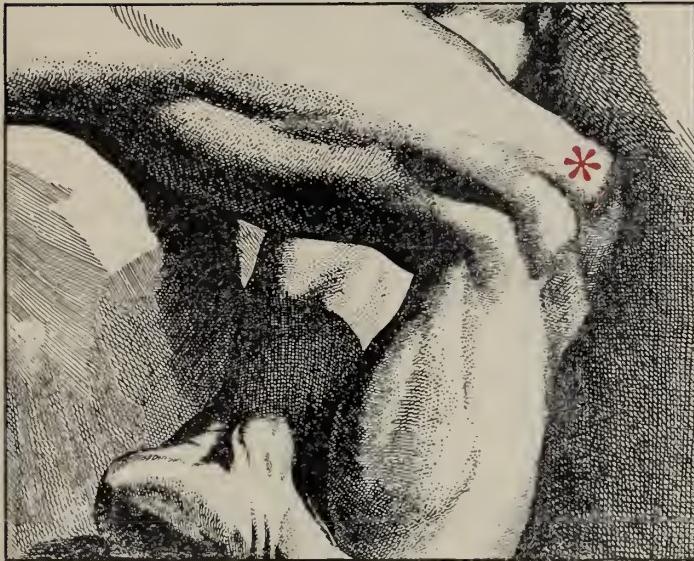
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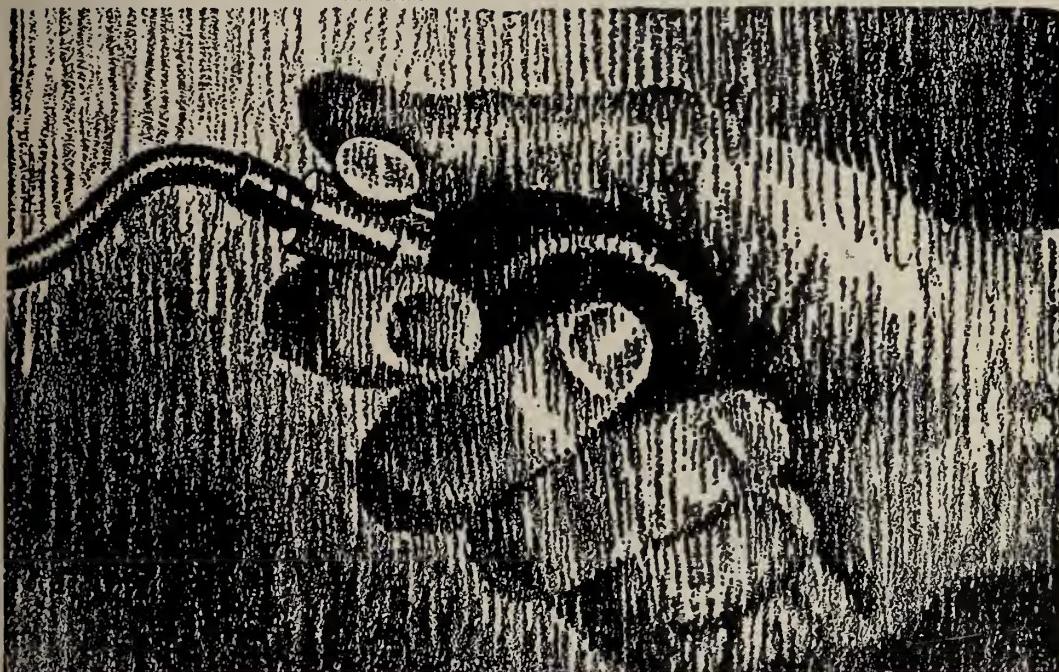
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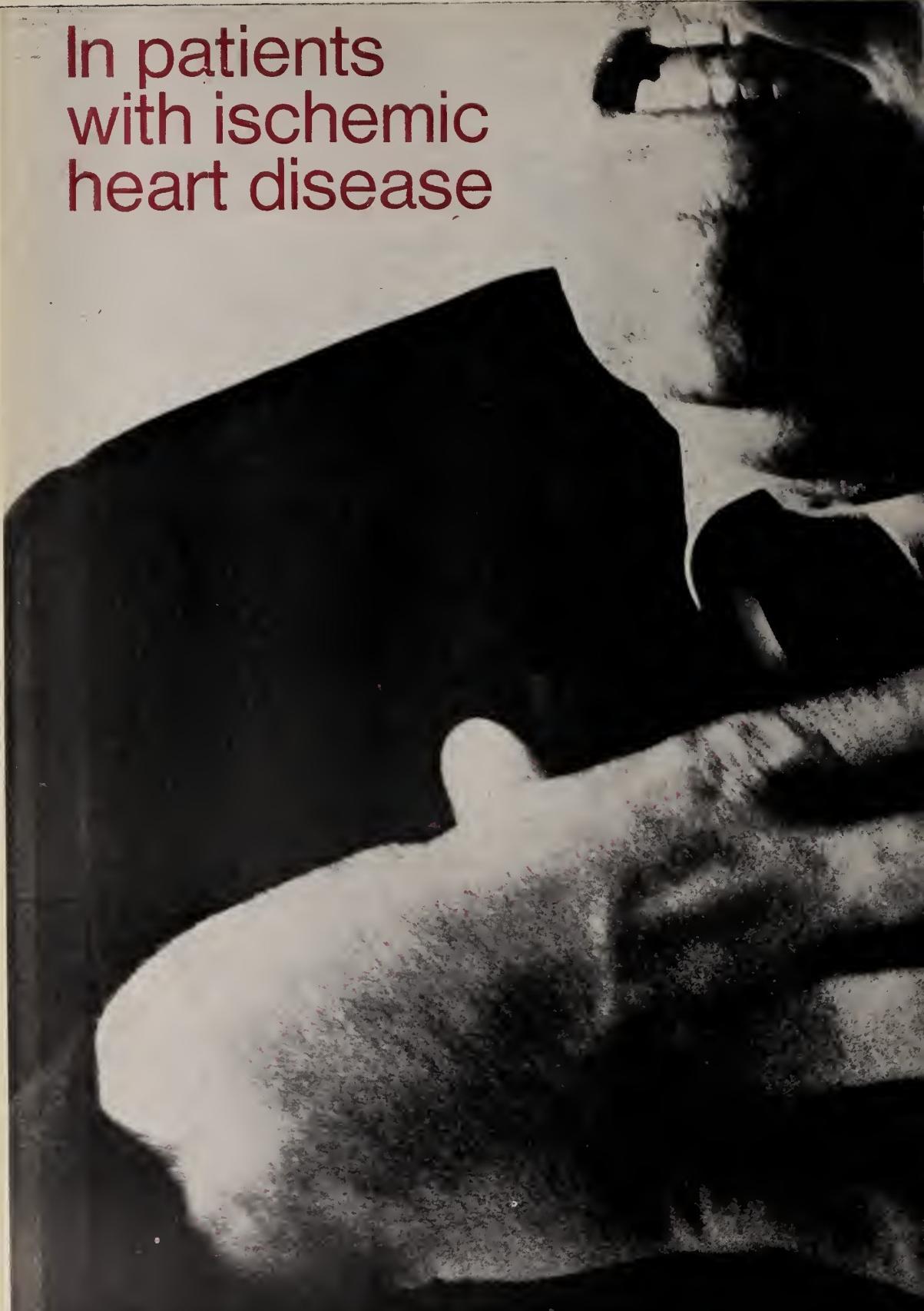
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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



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### Neumann, M., and Luisada, A. A.: Effect of Rapid- and Slow-Acting "Coronary" Drugs on Precordial Pain of the Aged. *Am. J. M. Sc.* 247:156, 1964.

Method: In a double-blind study, 33 elderly patients with chronic angina pectoris received placebo, dipyridamole 50 mg. t.i.d., and other coronary drugs, each for a 6-week period. The number of nitroglycerine tablets consumed in the last 2-week period was compared for each test preparation.

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1. Griep, A. H.: A Long-Term Therapy of Ischemic Heart Disease. *Angiology* 14:484, 1963.
2. Wirecki, M.: Dipyridamole: Evaluation of Long-Term Therapy in Angina Pectoris. *Current Therap. Res.* 5:472, 1963.
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## EVALUATION OF A NEW METHOD FOR THE DETERMINATION OF CHOLESTEROL IN BLOOD\*

A PRELIMINARY REPORT

ANGEL ALBERTO COLON, D.Sc., M.D., MARIO R. GARCIA-PALMIERI, M.D.,  
and EMILIO A. NAZARIO, M.S.

Since the publication by Liebermann<sup>1</sup> in 1885 and Burchard<sup>2</sup> in 1890 of a reagent made up of acetic anhydride and sulfuric acid which was suitable for the determination of sterols, there has practically been a mushrooming of methods for cholesterol determination based on this reagent. Prominent among said methods are those of Bloor,<sup>3</sup> later modified by Schoenheimer and Sperry<sup>4</sup> who introduced a digitonin precipitation prior to development of color with the Liebermann-Burchard (L-B) reagent. This method was promptly tested by Fitz<sup>5</sup> with good results and later by Hepburn and Kotlikoff.<sup>6</sup> In 1951 Sister M. Charlotte Zingg<sup>7</sup> reported on a study of many of the variables that affect the results in the determination of cholesterol using the L-B reagent. At present many laboratories are employing the Abell-Kendall<sup>8</sup> method which appeared in 1952.

Many other methods<sup>9,10,11</sup> not based on the L-B reagent have also been developed; nevertheless, the desirability of a fast and reliable method for cholesterol requiring but a single reagent has been in the minds of many investigators. Thus Ferro and Ham,<sup>12</sup> Huang, Chen, Webler, and Raftery<sup>13</sup> have recently published methods using a single reagent. It is the purpose of this communication to present our preliminary evaluation of the last mentioned method (Huang et al.) comparing it with the well established method of Bloor<sup>3</sup> which has been in use in our laboratory for many years.

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\* From the Department of Medicine of the School of Medicine of the University of Puerto Rico, San Juan, Puerto Rico. This work was supported in part by the Division of Collaborative Studies of the National Heart Institute under contract No. P. H. 43-63-620, and U. S. Army Contract No. D. A.-49-007-MD-946.

## MATERIALS AND METHODS

Venous blood was obtained from fifty patients selected at random in our wards. The blood was allowed to clot spontaneously and centrifuged at 2000 rpm for 10 minutes. The serum was then removed using fine tipped pipets, placed in a clean test tube, stoppered and stored in a freezer. For analysis the sera were removed from the freezer, allowed to thaw, shaken to insure homogeneity and samples withdrawn for analysis. Each serum sample was analyzed for total cholesterol by the methods of Huang and Bloor. As cholesterol standard, Pfanziehl C. P. cholesterol M.P. 147-148°C was used.

The reagent used in Huang's method is a mixture consisting of 30% glacial acetic acid, 60% acetic anhydride and 10% concentrated sulfuric acid by volume. It is saturated (2%) with anhydrous sodium sulfate. We usually prepare 700 ml of mixture at a time which is sufficient for about 50 tests.

To a one liter Erlenmeyer flask add 420 ml of acetic anhydride and place the flask in an ice bath until cold. Add slowly 210 ml of glacial acetic acid, mix thoroughly and keep in the ice bath. Carefully add 70 ml of concentrated sulfuric acid in 10-12 ml portions while twirling the flask. The cold acid mixture is then saturated with 14 grams of anhydrous sodium sulfate, transferred to a dark brown bottle and stored in the refrigerator. This mixture will keep well for three weeks.

**Huang's method:**

A blank and standard are required with the unknowns. Ten ml of the L-B reagent mixture are placed in a 25 ml glass stoppered graduated cylinder, and 0.4 ml serum added. The mixture is shaken thoroughly, and allowed to stand for 20 minutes. In a similar manner 0.4 ml of a cholesterol standard containing 2 mg/ml are added to the reagent. A blank of 0.4 ml of water and 10 ml of the reagent must also be prepared. Shortly before the 20 minutes required for color development are over, the samples are transferred to the cuvettes and the color intensities read at 610 m $\mu$  in a spectrophotometer against the water blank. The results are obtained either from a calibration curve or by the formula:

$$\frac{\text{O. D. sample}}{\text{O. D. standard}} \times 200 = \text{mg\% of cholesterol in sample}$$

**Bloor's method:**

Add 0.75 ml of serum to 20 ml of 3:1 alcohol-ether mixture

and allow to stand for one hour at room temperature (24-25°C). Dilute to 25 ml with the alcohol-ether mixture and filter. Immediately transfer 10 ml of the filtrate to a 30 ml beaker and evaporate on a hot plate at low heat.

Extract the residue three times with 1.5 ml portions of chloroform warming the beaker with each addition of chloroform. Transfer to a 25 ml graduated cylinder, cool and complete to 10 ml with chloroform. Add 4 ml of acetic anhydride and 0.2 ml of concentrated sulfuric acid. Mix at once and let stand for 10 minutes in the dark at 24-25°C. Read promptly at the end of the 10 minutes in a spectrophotometer set at 415 mu. The results are obtained directly from a calibration curve.

#### RESULTS

The results obtained in each of the 50 samples examined by the methods of Bloor and Huang are given in Table I.

TABLE I  
CHOLESTEROL VALUES OBTAINED BY THE BLOOR AND  
HUANG METHODS

Sample Number	Cholesterol mg%			Sample Number	Cholesterol mg%		
	Bloor	Huang	Diff. B-H		Bloor	Huang	Diff. B-H
1	213	217	-4	26	225	216	+9
2	270	262	+8	27	248	241	+7
3	267	263	+4	28	208	206	+2
4	225	232	-7	29	196	198	-2
5	251	250	+1	30	267	267	0
6	191	186	+5	31	206	201	+5
7	267	258	+9	32	201	204	-3
8	258	244	+14	33	201	201	0
9	320	309	+11	34	204	206	-2
10	267	258	+9	35	292	300	-8
11	258	244	+14	36	184	179	+5
12	352	352	0	37	288	292	-4
13	169	170	-1	38	218	222	-4
14	141	145	-4	39	170	169	+1
15	213	221	-8	40	222	225	-3
16	141	137	+4	41	117	113	+4
17	267	274	-7	42	174	168	+6
18	122	117	+5	43	127	124	+3
19	225	232	-7	44	202	196	+6
20	204	210	-6	45	134	129	+5
21	235	238	-3	46	230	222	+8
22	171	171	0	47	194	199	-5
23	251	258	-7	48	138	157	-19
24	242	238	+4	49	238	244	-6
25	244	251	-7	50	166	167	--1

## DISCUSSION

In our experience ten samples plus one blank and one standard may be conveniently analyzed in one batch. We prefer to analyze the ten samples, blank and standard in 25 ml glass stoppered graduated cylinders containing 10 ml of the L-B reagent. As each sample is added to the reagent it is immediately mixed. This operation can and should be done for the ten samples in less than five minutes. The blank and standard are added to the first and second cylinders and as soon as the standard is mixed with the reagent a timer is set for 20 minutes. After this interval the samples are read in a spectrophotometer at 310 mu. We have found that the color is stable for an additional five minutes. The samples must, therefore, be read within this period.

With adequate facilities one technician can do twenty samples in one hour.

The L-B reagent is kept in the refrigerator where it is stable for three weeks. When needed it is removed from the refrigerator and allowed to warm up to about 22°C before using.

We try to have the samples and the standard at 23-24°C when they are mixed with the L-B reagent. This may be attained either in an ice-cooled bath or in a room with air-conditioning. It has been our experience that higher temperatures may result in slightly lower results and lower temperatures in slightly higher values.

## CONCLUSIONS

The means for the two methods were 215.6 mg% for results by Bloor's method and 215.2 mg% by Huang's. The difference between the two means is not significant. The standard deviation was found to be 49.6 for the results by Bloor's method and 49.8 by Huang's method again indicating that there is no significant difference between the results obtained by the two methods.

For a series of 50 values (49 degrees of freedom) there is a probability of 95% that the "t" distribution will yield a value of 1.676 at 5% significance level. Actually the results obtained from the differences between the two methods showed a value of "t" = 0.09. This value compared with the expected value of 1.676 indicates that there is no significant difference between the two methods.

It appears from this preliminary study that the two methods give comparable results. Further evaluation in other laboratories of this simple and rapid method seems warranted.

## SUMMARY

The single-reagent, rapid method of Huang et al. for the determination of serum cholesterol was compared with that of Bloor. Statistical treatment of our sample showed that the two methods give comparable results, the differences being not significant. With adequate facilities one technician can perform twenty determinations in one hour. It is recommended that further study be carried out in other laboratories in view of the simplicity, rapidity and apparent reliability of the method.

## RESUMEN

El rápido método de Huang et al. para la determinación de colesterol en suero empleando un reactivo único ha sido comparado con el de Bloor. El examen estadiático demostró que los métodos dieron resultados comparables y las diferencias entre ellos no fueron significativas. Con facilidades adecuadas un técnico puede efectuar veinte determinaciones en una hora. Una breve descripción de los dos métodos ha sido incluida. Se sugiere que otros laboratorios efectúen estudios sobre el método en vista de su rapidez, sencillez y aparente confiabilidad.

## ACKNOWLEDGMENT

We wish to express our appreciation to Mrs. Ofelia Beléndez for her assistance in undertaking some of the laboratory determinations and to Mr. Jaime López López for the statistical examination of the results.

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## "THE USE OF SU 4885 (METHOPYRAPONE) TO STUDY THE PITUITARY ACTH RESERVE IN PATIENTS WITH SHEEHAN'S DISEASE AND PITUITARY TUMORS"

LILLIAN HADDOCK, M.D. and OVIDIO RODRIGUEZ, M.D.\*

A series of compounds that inhibit the adrenocortical enzyme systems concerned with the hydroxylation of the steroid molecule, have been shown to suppress hydrocortisone production in man. These compounds include amphenone, perthane and methylenedianiline all chemically related to the insecticide D.D.T. Recently Chart and coworkers modified the chemical structure of Amphenone, a highly toxic adrenal inhibitor which blocks 11,-17 and 21 hydroxylation of progesterone to form a dipyridyl propanone investigated as SU 4885 and available for clinical use as Methopyrapone.

Liddle and coworkers<sup>1</sup> in the clinical evaluation of SU 4885, paradoxically found that with prolonged oral or intravenous administration of the compound there occurred after several hours a marked increase in the level of plasma 17 hydroxycorticoids, urinary 17 hydroxycorticoids and urinary 17 ketosteroids. Steroid chromatography of the plasma and urine showed an increase in the level of 11-desoxy-cortisol, desoxycorticosterone and their metabolites, a steroid pattern similar to that found in children with hypertensive congenital adrenal hyperplasia as described by Eberlein and Biogiovanni.<sup>2</sup> The metabolic alteration in this type of adrenogenital syndrome is an enzymatic defect in 11 Beta hydroxylation of the adrenal steroids impairing thus the synthesis of hydrocortisone. Liddle, thus postulated that SU 4885 might act as an inhibitor of adrenocortical 11 Beta hydroxylase. This was proved when he obtained through "in vitro" studies a complete inhibition of the activity of a partially purified 11 Beta hydroxylase derived from bovine adrenal tissue when added to a  $1.5 \times 10^{-5}$  molar solution of SU 4885.

By inhibiting 11-Beta hydroxylation SU 4885 blocks the synthesis of hydrocortisone. Since hydrocortisone is the hormone of principal importance in regulating the secretion of adrenocorti-

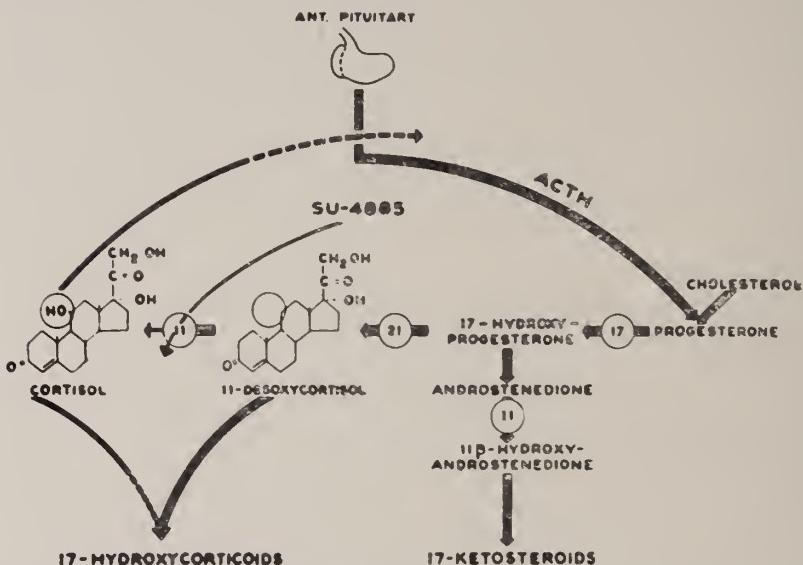
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From the Endocrine Section of the Department of Medicine of the University of Puerto Rico School of Medicine. This investigation was supported by Grant Number (5 TI AM 5097-7) from the National Institute of Arthritis and Metabolic Diseases. SU 4885 was generously supplied by Dr. C. H. Sullivan, Ciba Pharmaceutical Products Inc.

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\* Trainee in Endocrinology and Diabetes. (5 TI AM 5097-7)

cotropin in man, a fall in hydrocortisone produces a compensatory increase in ACTH secretion. The increase in ACTH would increase the adrenocortical secretion of 11-desoxycorticosteroids, including compound S., desoxycorticosterone (DOCA) and certain 17 ketosteroids. Figure 1 demonstrates the site of action of Methopyrapone or Metopirone.



**—Site of action of SU-4885:** Partial inhibition of cortisol synthesis results in release of pituitary ACTH and increasing secretion of 11-desoxycortisol, a poor ACTH suppressant. The consequent rise in urinary 17-hydroxycorticoids may be estimated as 17-ketogenic steroids or as Porter-Silber chromogens.

Figure 1.—Site of Action of Methopyrone (Gold, E. M., Dr. Raimundo V. C. and Forsham P. H. J. C. E. M. 9, 1960).

Liddle introduced the use of SU 4885 as an agent to test the pituitary ACTH reserve.<sup>3</sup> He showed that when administered to normals there was a two to fivefold increase in the urinary excretion of 17 hydroxycorticosteroids which was detected on the same day of its administration when given intravenously and the day after its administration when given orally. Gold and associates<sup>4</sup> showed that the determination of the urinary 17 ketogenic steroids was a better parameter to measure the Methopyrapone response than the urinary 17 hydroxycorticosteroids and 17 ketosteroids. After Methopyrapone administration there is a marked increase in urinary corticoids. However little or no significant change from control values is seen to occur in the excretion of cortisol metabolites. The major component of the  $C_{21} O_4$  fraction is identified as the tetrahydroderivative of 11 desoxycortisol. Conventional modification of the Porter Silber method for urinary 17 hydroxy-

corticosteroids fails to recover from 25-30% of tetrahydro 11 desoxycortisol from the urine. In addition the extra adrenal handling of desoxycortisol differs from that of cortisol (hydrocortisone) and approximately 35% of the former is excreted reduced in the C<sub>20</sub> position.<sup>5</sup> This 20 O1 metabolite can be estimated as a 17 ketogenic steroid but not as a Porter Silber chromogen. Thus, the urinary levels of the metabolites of 11 desoxycortisol can be best detected by its direct determination or by oxidative conversion to a 17 ketosteroid with sodium bismuthate. The 17 hydroxycorticosteroids which upon oxidation with sodium bismuthate are converted to 17 ketosteroids comprise the 17 ketogenic steroids.

Recently Kaplan<sup>6</sup> has shown that the direct determination of 11 desoxycortisol in the plasma and its metabolites in the urine are the most satisfactory parameter to differentiate most clearly the normal and abnormal response to Methopyrapone.

A normal response to Metopirone after its oral administration will produce a 2 to 5 fold increase in the urinary 17 hydroxycorticosteroids<sup>4,7</sup> and a two to fourfold increase in the urinary 17 ketogenic steroids.<sup>8</sup>

The present report compares the endogenous pituitary ACTH reserve in 8 patients with Sheehan's syndrome and 4 patients with pituitary tumors using the 17 ketogenic steroids, the 17 hydroxycorticosteroids and the 17 ketosteroids as parameter to measure the Methopyrapone response.

#### MATERIALS AND METHODS

**Subjects:** Twelve patients were studied. Eight patients had Sheehan's disease and all exhibited clinical and laboratory evidence of hypogonadism, hypothyroidism and hypoadrenalinism. Table I summarizes the clinical findings in these 8 patients. Four patients, one male and three female, had pituitary tumors. Table II summarizes the clinical findings in these 4 patients. Patient A. C. was studied five years, after being irradiated and when the tumor was active. The tumor was irradiated again in 1962 and she was re-evaluated one week and 18 months after the second irradiation treatment. In the latter evaluation she still showed mild hypercalcemia and hypercalciuria which may still denote activity of the tumor.<sup>9</sup>

**Test Procedure:** The Metopirone tests were performed according to the schedules recommended by Liddle et al<sup>3</sup> for the oral procedure, i.e., 750 mg every 4 hour for 6 doses. The maximum response is usually observed the day after the Metopirone administration. 24 hour urine specimens were obtained on the 2 days preceding the test the day of and the day after the admi-

TABLE I  
ENDOCRINOLOGIC EVALUATION OF  
EIGHT PATIENTS WITH SHEEHAN'S DISEASE

	H. A.	F. R.	R. R.	B. M.	A. F.	C. N. B.	N. M.	V. M.
Age	40	43	42	50	37	57	52	40
Parity	XV	X	V	VII	XI	VIII	III	IX
Duration of Illness	10 yrs.	3 yrs.	7 mos.	12 yrs.	4 mos.	22 yrs.	16 yrs.	2 mos.
Cause of Bleeding	Retained Placenta	Placenta Previa	Abruption Placenta	Retained Placenta	Retained Placenta	Retained Placenta	Retained Placenta	*Subarachnoid Hemorrhage
Shock	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Lactation	No	No	No	No	No	No	2 weeks (scanty)	No
Loss of libido	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Amenorrhea	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Genital Atrophy	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Loss of body hair	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Cold intolerance	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Myxedematous facies	Yes	No	No	No	No	Yes	No	No
Weight loss	No	Yes	No	Yes	Yes	No	No	Yes
Hypoglycemia	No	Yes	No	No	No	Yes	No	No
Electrolyte disturbance	No	No	No	No	No	No	No	No
Complicating illness	Chronic Pyelonephritis			Pyelonephritis Old TBC Bronchiectasis	Myxedema Heart Disease Cardiac Cirrhosis	Schistosomiasis Portal Hypertension		

\* V. M. had a Subarachnoid Hemorrhage in the 5th. month gestation and a Bacteremic shock in the 7th. month of her pregnancy.

## ENDOCRINOLOGIC EVALUATION OF EIGHT PATIENTS WITH SHEEHAN'S DISEASE (Cont. Table I)

	H. A.	F. R.	R. R.	B. M.	A. F.	C. N. B.	N. M.	V. M.
Thyroidal 24 hr.	Pre TSH	11.7	--	4.0	16.0	11.9	PBI	7
I-131 Uptake (%)	Post TSH	26	--	22.2	23.4	30.2	2.7 mcgm %	--
Serum Cholesterol (mg.%)		218	205	206		288	142	243
Glucose Tolerance Test	Flat	flat	flat	flat	flat	flat	flat	flat
Serum Na (mEq/L)		140.0	125.0	143.8	128.6	141.0	139.0	145.8
Serum K (mEq/L)		4.4	3.9	5.0	4.5	4.3	4.5	4.4
Urinary 17 ketosteroids (mg./d)		2.0	0.57	3.5	1.0	3.7	1.5	0.77
Urinary 17 OH Steroids (mg./d)		0.65		1.02	1.4	0.7	1.2	0.91
Urinary 17 Ketogenic Steroids (mg./d)		----		2.4	10.5	5.8	1.3	6.8
Pituitary ACTH Reserve	*KGS not done	Yes	Yes	No	Yes	No	No	limited
Adrenal Reserve	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

\* 17 Ketogenic steroids not done.

TABLE II — ENDOCRINOLOGICAL EVALUATION IN 4 PATIENTS WITH PITUITARY TUMORS

	N. T.	J. C.	T. M.	1	A. C.
Age	14	34	49	52	2
Sex	F	M	F	F	F
Type of Tumor	Craniopharyngioma	Eosinophilic Adenoma (inactive)	Eosinophilic Adenoma (active)	Eosinophilic Adenoma	Eosinophilic Adenoma (active?)
X-Ray Evidence of sellar erosion	Yes	Yes	Yes	Yes	Yes
Previous Pituitary Irradiation	No	One year Post irradiation	No	5 yrs. prior	One week Post irradiation
Thyroidal 24 hr.	Pre TSH	35.0	29.3	6.7	18 Months Post irradiation
I-131 uptake (%)	Post TSH	23.3	25.2		9.8
Urinary 17 ketosteroids (mg./d)	0.97	7.0	4.7	2.8	23.1
Urinary 17 OHcorticosteroids (mg./d)	0.4	5.0	6.1	3.6	3.3
Urinary 17 ketogenic steroids (mg./d)		14.3	16.5	5.7	5.0
Pituitary ACTH Reserve	limited	Excellent	Excellent	Excellent	Excellent
Adrenal Reserve	limited	Excellent	Excellent	Excellent	Excellent

nistration of Metopirone. After a 3 to 4 day rest period 40 units twice a day of ACTHAR Gel were given intramuscularly for 4 days. The administration of ACTH prior or after the administration of Methopyrapone did not alter the Methopyrapone response.

**Steroid Assays:** The urinary 17 hydroxycorticosteroids were determined as Porter Silber chromogens by the method of Nelson and Samuels,<sup>10</sup> the urinary 17 ketosteroids by the method of Callow<sup>11</sup> and the urinary 17 ketogenic steroids by an adaptation of the Norymberski procedure.<sup>12</sup> Our normal values for these steroid assays are as follows: urinary 17 ketosteroid: female 2.3-10.6 mg./d male 3.2-12 mg./d; urinary 17 hydroxycorticosteroids: female 2.3-8.1 mg./d male 2.5-12 mg./d; urinary 17 ketogenic steroids: female 6.6-12.8 mg./d., male 8.3-21.1 mg./day.

#### RESULTS

When the urinary 17 ketosteroids were used as parameter to study the response to Methopyrapone, none of the eight cases with Sheehan's disease showed an increase from the basal level after Methopyrapone administration (Fig. 2). Using the urinary 17 hydroxycorticosteroids, one patient, V.M., is found to have an ade-

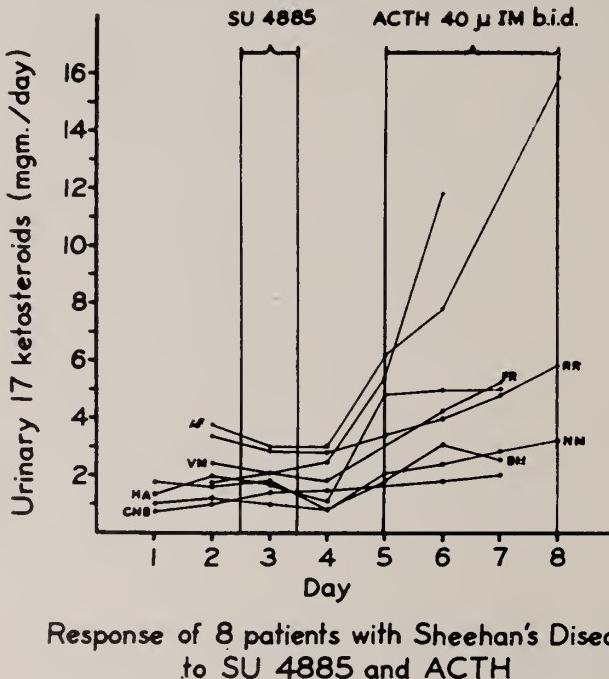


Figure 2.—Using the urinary 17 ketosteroids as parameter to study the Methopyrapone response no pituitary ACTH reserve is detected and in 6 patients (C. N. B., H. A., B. M., N. M. R. R. and F. R.) the adrenal reserve, when using this parameter is very limited.

quate pituitary ACTH reserve, as shown by a twofold increase in the urinary 17 hydroxycorticosteroids the day after Methopyrapone administration (Fig. 3). This patient was studied two months post-partum and four months after developing the clinical picture of Sheehan's disease. Upon determination of the urinary 17 ketogenic steroids in 6 of these patients 4 subjects (P. R., N. M., F. R. and A. R. F.) are found to have an adequate endogenous pituitary ACTH reserve as shown by a two to three fold increase in the urinary 17 ketogenic steroids the day after Methopyrapone administration (Fig. 4). These patient's basal levels of urinary hydroxysteroids (1.02-1.4 mg/d) were fair and about half the normal value, thus it was to be expected for them to have some endogenous pituitary ACTH reserve. The urinary 17 ketogenic steroids were not done in V. M. and H. A. but V. M. had shown some reserve using the urinary 17 hydroxycorticosteroids as parameter. This goes along with our clinical observation that many of the patients with Sheehan's disease prior to their recognition have gone through surgical procedures and acute illness without going into adrenal crisis. Liddle,<sup>3</sup> Holub,<sup>8</sup> and Gold,<sup>13</sup> have encountered patients which have a limited or no pituitary ACTH reserve when tested with

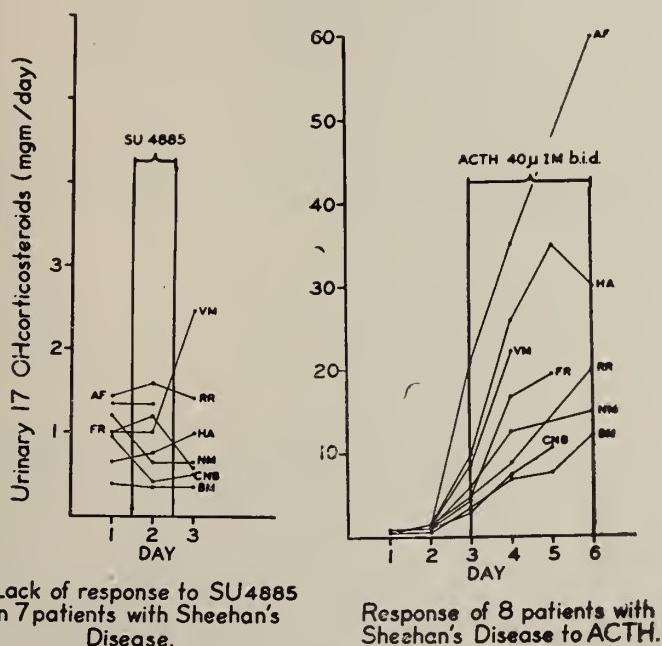


Figure 3.—Using the urinary 17 hydroxycorticosteroids as parameter to study the Methopyrapone response no pituitary ACTH reserve is detected in 7 patients with Sheehan's disease. The adrenal reserve is excellent in all the cases.

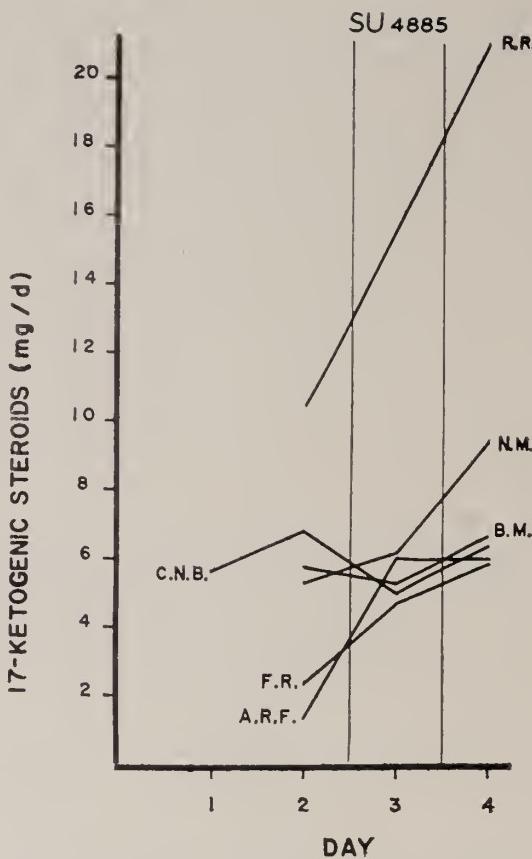


Figure 4.—Using the urinary 17 ketogenic steroids as parameter to study the Methopyrapone response in 6 patients with Sheehan's disease 4 subjects are shown to have an adequate reserve.

Methopyrapone, but who upon undergoing surgery a good reserve is encountered. Thus, these patients may have even a higher reserve were they exposed to more stressful situations such as surgery.

The ability of the adrenals of these patients to respond to exogenous ACTH was excellent regardless of the duration of the disease. This is shown by a very marked increase in the urinary 17 hydroxycorticosteroids after ACTH administration (Fig. 3).

In figure 5 is shown the response to Methopyrapone of the 4 patients with pituitary tumors using the urinary 17 hydroxycorticosteroids as parameter. An excellent pituitary ACTH reserve was found in the three acromegalic patients as shown by a three to eight fold increase in the urinary 17 hydroxysteroid the day after Methopyrapone administration. In A. C. the pituitary ACTH reserve is improved one week after the second irradiation to the

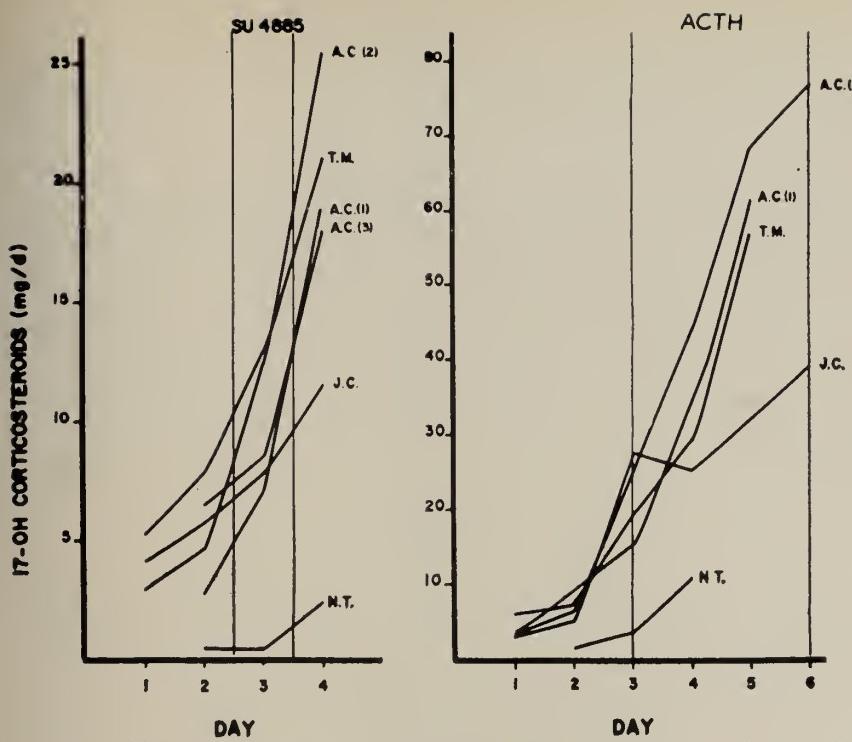


Figure 5.—The response to Methopyrapone and ACTH in 4 patients with Pituitary Tumors using the urinary 17 hydroxycorticosteroids as parameter.

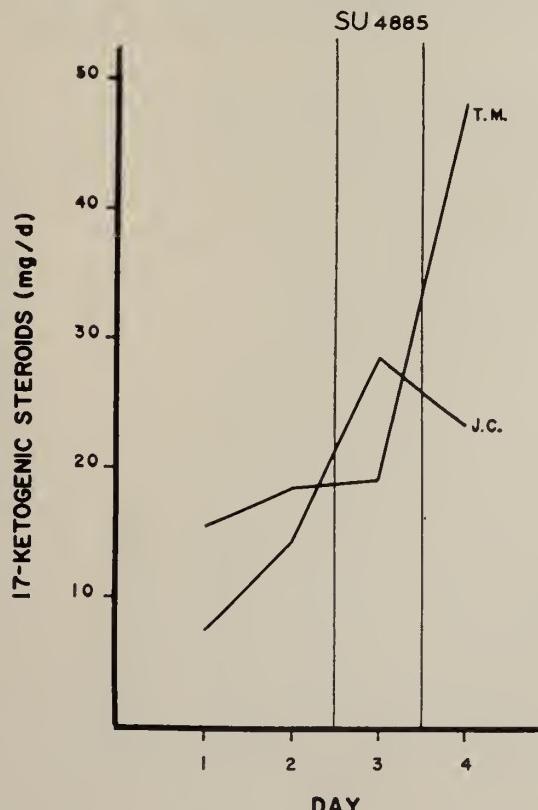


Figure 6.—The response to Methopyrapone in 2 acromegalic patients using the urinary 17 ketogenic steroids as parameter.

pituitary. When studied 18 months later the basal urinary hydroxysteroids are higher but the endogenous pituitary ACTH reserve is similar to that on the first study prior to the second irradiation. The female patient with a Craniopharyngioma had a very limited pituitary ACTH reserve. In two of the acromegalic patients the excellent endogenous pituitary ACTH reserve is again shown using the urinary 17 ketogenic steroids as parameter (Fig. 6). The adrenal reserve of the 3 acromegalics was excellent but that of N. T., the female patient with craniopharyngioma, was limited (Fig. 5).

#### DISCUSSION

With the synthesis of SU 4885, a rather innocuous adrenocortical enzyme inhibitor, the pituitary adrenocortical relationship in man can be elucidated in a quantitative reproducible manner. The response to this compound is studied by measuring in the urine and plasma the level of 11-desoxycortisol and its metabolites as Porter Silber chromogens (17 hydroxycorticosteroids), 17 ketogenic steroids and 17 ketosteroids. The best parameter are the 17 ketogenic steroids and the 11-desoxycorticosteroids. Maximal steroidogenesis can be obtained by administering the doses hereby used.

The side effects of methopyrapone are minimal. If given orally it may produce epigastric discomfort, nausea, vomiting and diarrhea. These local effects in the gastrointestinal tract can be avoided by giving foods and antacids concomitantly. When given in doses of 60 mg/Kg intravenously Gold<sup>1</sup> encountered thrombo-phlebitis in 3 patients. This can be avoided by giving the dose recommended, 30 mg/Kg. The oral test has been shown to be by far easier to perform and more informative than the intravenous test and has been amply recommended. Meakin and co-workers<sup>14</sup> report an episode of adrenocortical insufficiency after SU 4885 administration in a nephrotic woman who had been on prolonged steroid therapy. As a precaution the blood pressure should be checked frequently and evidence of adrenal insufficiency should be looked for carefully. Except for occasional nausea, we did not encounter any serious side effects in our patients.

Our clinical experience in the use of this compound to attest Pituitary ACTH reserve in patients with panhypopituitarism and pituitary tumors compares with that of other investigators. Liddle<sup>3</sup> using the urinary 17 ketosteroids and 17 hydroxycorticosteroids as parameter to measure the response to Methopyrapone, encountered absent pituitary ACTH reserve in 2 patients with Sheehan's disease, and limited to good ACTH reserve in patients with various

endocrine tumors. In studying 9 patients with chromophobe adenomas he encountered limited pituitary ACTH reserve in 6 patients that either had received Pituitary irradiation or had had a subtotal resection of the adenoma. All these patients were able to respond normally to exogenous ACTH. The same experience was encountered in patients with eosinophilic adenomas. Kaplan<sup>6</sup> compared the response to Methopyrapone in normal volunteers and patients with pituitary disease using the urinary 17 hydroxycorticosteroids and the urinary 11 desoxycorticosteroids, as parameters. In 4 patients with Shehan's disease he showed no pituitary ACTH reserve in 2 patients and a limited reserve in 2 patients using the urinary 17 hydroxycorticosteroids as parameter to measure the response of Methopyrapone. When he used the urinary 11 desoxycorticosteroids as parameter one of the patients who had shown no reserve using the urinary 17 hydroxycorticosteroids showed an adequate pituitary ACTH reserve. In this latter patient the basal level of urinary 11 desoxycorticosteroids was undetectable but rose to 2.5 mg/day the day after Methopyrapone administration. His experience with the patients with chromophobe adenomas and Acromegaly compares with that of Liddle using both assays, the 17 hydroxycorticosteroids and the 11 desoxycorticosteroids as parameters, appearing the response more striking with the latter assay.

In Gold's experience<sup>13</sup> expanding pituitary tumors markedly reduced the rise in 17 ketogenic steroids following SU 4885 administration with the exception of those secreting excessive amounts of Growth hormone. In studying 7 patients with active acromegaly he found good pituitary reserve in 6 patients and a limited pituitary reserve in 1 patient. Three months after pituitary irradiation in the above six cases the response to Methopyrapone was diminished. He states that the eradication of a normal response by irradiation may prove useful for assessing the efficacy of therapy. He explains the better response seen in Acromegaly as compared with the non functioning tumors as due to: (1.) the striking physical changes seen because of excessive growth hormone secretion may cause acidophilic tumors to be detected earlier than are non functioning intrasellar tumors and (2) that growth hormone or an enhanced hypersecretion of Corticotropin may maintain or even enhance adrenocortical sensitivity thereby augmenting the response to SU 4885 even when the reserve of Pituitary Corticotropin has been limited by the tumor.

Molinatti<sup>9</sup> compared the response to Methopyrapone in seven acromegalics before and sometime after implantation of the pituitary with Ytrium 90 using the urinary 17 hydroxycorticosteroids as parameter. A normal response to the administration of

Methopyrapone was found after implantation of the pituitary in 4 cases and a limited response in 3 patients. In one of the latter patients when tested 5 months after pituitary implantation the pituitary ACTH reserve was greater than before. He also showed that in spite of the abolishment of the increased somatotropic activity obtained in all the treated patients almost no changes were found in the other pituitary functions and hence in the dependent endocrine glands. On the other hand, in some cases pre-existing endocrine deficiencies improved or disappeared after the operation. His findings compare with ours in patient A. C.

Further studies conducted by these authors and others have shown limited to absent pituitary ACTH reserve in patients with Addison's disease, cachectic states secondary to anorexia nervosa and chronic debilitating illness, and after prolonged steroid therapy. Excellent pituitary ACTH reserve has been shown in patients with Cushing's syndrome due to hyperplasia and none in patients with tumors. The fact that patients with adrenal hyperplasia respond vigorously to SU 4885 whereas those with adrenal tumors do not is consistent with the view that the former are only quantitatively different from normals, whereas the latter are qualitatively different from normal with respect to homeostatic regulation of adrenal function. In children with hypertensive congenital adrenal hyperplasia Liddle has shown a further increase in urinary 17 hydroxycorticosteroids, meaning that the defect of 11-Beta hydroxylation in these patients was partial.<sup>3</sup>

It has been stressed by Liddle,<sup>3</sup> Kaplan<sup>15</sup> and others that the results of the Metopirone test might not agree with other evidences of pituitary ACTH secretory capacity. Kaplan<sup>15</sup> compared the Metopirone test with one available test of pituitary ACTH secretion, the insulin tolerance test. He compared the response to these two tests in patients with normal and abnormal pituitary function. His results indicated that the Metopirone test may be abnormal when the response to the stress of hypoglycemia is normal. His findings suggest, as he states, that this test should not be taken as a true measure of total ACTH "reserve", but rather as a measure of only one aspect of pituitary ACTH secretory capacity the ability to increase ACTH release after a fall in circulating hydrocortisone.

#### CONCLUSION

In summary we have presented our experience and that of others in studying pituitary ACTH reserve using Methopyrapone in patients with panhypopituitarism and pituitary tumors. We have presented data supporting the fact that the determination of

the urinary 17 ketogenic steroids and 11 desoxycorticosteroids are the best parameters in evaluating the response to Methopyrapone.

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#### RESUMEN

En resumen hemos presentado nuestra experiencia y la de otros investigadores en el uso de Metopirona para estudiar la reserva pituitaria de Corticotropina en pacientes con la enfermedad de Sheehans y con tumores pituitarios.

Se ha presentado evidencia de que la determinación de los niveles urinarios y plasmáticos de los esteroides 17 quetogénicos y 11 desoxicorticosteroides son los mejores parámetros para evaluar la respuesta a Metopirona.

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## "STRICTLY POSTERIOR" MYOCARDIAL INFARCTION\*

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The main cause of death in Puerto Rico at present is heart disease and coronary heart disease is the principal etiological agent as the cause of death of Puerto Rican cardiac patients.<sup>1</sup>

The use of the electrocardiogram (EKG), the use of laboratory aids such as the determination of elevated specific serum enzymes and the better understanding of the clinical picture of acute myocardial infarction has increased the percentage of pre-mortem diagnosis of this serious disease. In spite of these advantages in clinical and technical knowledge some cases of myocardial infarction are still never diagnosed by the clinician with consequent detriment to the patient.

With the advent of vectorcardiography the number of cases of myocardial infarction that go undiagnosed in our hospital has been lowered. The vectorcardiogram (VCG) provides an accessible means of identifying the electrical events in the activation of the heart muscle in sequence and viewed from the horizontal, sagittal and frontal planes. Areas of myocardial necrosis are electrically inert and the vectorcardiogram loop will be distorted from the normal configuration in the areas where the infarction of the cardiac muscle has occurred. Hence, the VCG may aid in the diagnosis and localization of the infarcts of the myocardium which may go otherwise undetected.

The electrocardiographic criteria of myocardial infarction is the presence of abnormal Q waves. These Q waves are secondary to the loss of electrical forces in the infarcted area. As the infarcted segment of the myocardium becomes electrically inert, the area of myocardium opposite to it contributes electrical forces directed away from the area of necrosis.

The unbalanced forces of the remaining healthy tissue produce the Q wave characteristic of myocardial infarction in the leads facing the infarct.<sup>2</sup>

There are some infarctions which because of their location do not show Q waves in the EKG. An example of this is the infarction located in the posterior or dorsal wall of the left ventricle. A definite anatomical distinction should be made between these "strictly posterior" myocardial infarctions and the more frequent and obvious inferior or diaphragmatic ones which were pre-

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viously known as posterior infarctions. The term "strictly posterior" myocardial infarction is used when the affected area of myocardium is localized in the posterior wall of the left ventricle, beneath the left atrium and facing partially toward the left shoulder. What was erroneously called posterior myocardial infarction in the past is the one affecting the apical wall of the left ventricle that faces the diaphragm. This infarction is now known as diaphragmatic or inferior myocardial infarction.

In "strictly posterior" infarctions there is loss of the normal forces directed toward the back. The loss of these forces will leave the anteriorly directed ones unchecked with a consequent increase in their recorded magnitude. On the EKG, this increase in forces is recorded as tall R waves in  $V_1$  and  $V_2$  with a positive, tall T wave and ST vector directed posteriorly.<sup>2</sup>

The electrocardiographic picture in the precordial leads of this entity may be confused with that of right ventricular hypertrophy and with incomplete, atypical right bundle branch block. The purpose of this report is to demonstrate the value of the VCG in establishing the diagnosis of direct posterior myocardial infarction and distinguishing it from other causes of prominent R waves in the right precordial leads.

The Sanborn vectorcardiograph used at the University Hospital records the sequential electrical phenomena of myocardial activation by the cube system.<sup>3</sup> The depolarization and repolarization of the heart muscle may be recorded from the horizontal, the right sagittal and frontal planes. The normal VCG (Fig. 1)



Fig. 1 — Normal Vectorcardiogram.

presents three main loops. A very small, almost imperceptible P loop representing the atrial activation, a very large and prominent QRS loop that represents the ventricular activation and a small T loop which is the representation of the repolarization of the heart muscle. The point from where all these loops originate is called the "E" point and a line drawn from this point to the one most distal to it in the inscribed loop is known as the mean electrical axis of the corresponding loop.

The horizontal plane of the VCG corresponds to the precordial leads of the EKG. In it, the electrical events are recorded as they propagate anteriorly and to the right; then counterclock-

wise to the left and finally posteriorly. The loop is smooth and oval in shape. The QRS axis in the horizontal plane falls in the -30 to +30 range.

The sagittal plane of the VCG corresponds to the esophageal and aVF leads of the EKG. In it, the electrical events are inscribed as the vectors move slightly superiorly and anteriorly, then frankly inferiorly and finally posteriorly to return to the original point of departure. The whole loop is inscribed in a clockwise manner and the QRS axis may be anywhere between +100 to +70, but usually somewhere near +85.

The frontal plane of the VCG corresponds to the bipolar limb leads of the EKG. The vectors are inscribed as they move slightly superiorly and to the right, then frankly inferiorly and to the left to return to the point of origin. The axis falls in the range of 0 to +60. If the axis is from 0 to +40, the loop runs in a counterclockwise fashion. If the axis falls between +40 to +60 a clockwise loop is inscribed. The centripetal limb or initial portion of the QRS loop may normally cross over the centrifugal or final one forming a figure of eight pattern.

The T loop is normally found within the larger QRS loop and usually running nearly parallel to the axis of the QRS loop in the corresponding plane.

It is important to note that the normal QRS loop always ends exactly at the point of origin. When this is not so, an ST vector is formed which corresponds to a line drawn from point E to the point where the centripetal limb of the QRS ends. The direction of the vector determines the magnitude and direction of the ST changes in the clinical EKG.

## Material and Methods

Electrocardiograms of 250 cases of myocardial infarction treated in the University Hospital from January 1, 1961 to January 31, 1964 were reviewed looking for findings suggestive of "strictly posterior" myocardial infarction. All of the hospitalized patients had the diagnosis of myocardial infarction proven by a compatible clinical history and EKG and enzyme studies. Patients with right ventricular hypertrophy, pulmonary infarction and chronic pulmonary disease were eliminated from the study by proper clinical, laboratory and roentgenologic studies. Of the total number of cases there were 14 with electrocardiographic findings suggestive of this condition. VCG's were done on these subjects with the Sandborn vectocardiograph employing the cube reference system of Grishman and Scherlis.<sup>2</sup> Six cases were diagnostic of "strictly posterior" myocardial infarction.

## Results

In all the cases of strict posterior myocardial infarction there were characteristic configurations of the QRS loop that helped to distinguish these cases from those of right ventricular hypertrophy or right bundle branch block.<sup>4</sup>

In the horizontal plane, the QRS loop was initially inscribed to the right and more anteriorly than normal. The rest of the centrifugal limb ran in a nearly normal fashion but as the loop reached the most distal leftward point, the centripetal limb was distinctly abnormally displaced anteriorly as it moved to the right, back to point of origin (Fig. 2).

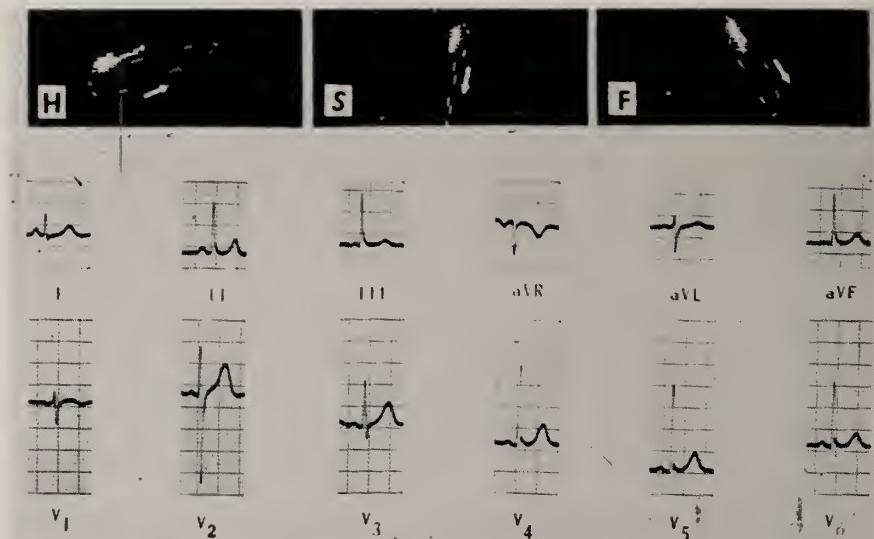


Fig. 2 — Vectorcardiogram and electrocardiogram of strictly posterior myocardial infarct. Note prominent R wave on  $V_1$  and upright T wave on EKG.

The most striking abnormality in the sagittal plane was the initial displacement of the centrifugal limb anteriorly and slightly inferiorly (Fig. 2). This corresponds to the changes already described in the horizontal plane.

In the frontal loop, no significant abnormalities are noted.

The T loop in our cases was oriented anteriorly and ran nearly parallel to the QRS axis.

These VCG findings correlate well with those of the EKG (Fig. 2). The QRS axis in the frontal plane was normal. A prominent R wave was seen in  $V_1$  with a positive T wave.

## Comments

The diagnosis of "strictly posterior" myocardial infarction by EKG alone is difficult because no significant Q waves are identi-

fied in the tracing. Furthermore, the tall R waves usually seen in the right precordial leads in this condition often leads the interpreter to the diagnosis of possible right ventricular hypertrophy or an atypical form of right bundle branch block. Several clues present in the EKG may hint to the interpreter that he is dealing with a "strictly posterior" myocardial infarction. Only after VCG analysis can one be reasonably certain of this diagnosis.

The clinical picture of myocardial infarction with EKG evidence of tall R wave in  $V_1$  and depressed ST segment and upright T wave in the right precordial leads should lead one to strongly suspect "strictly posterior" myocardial infarction. Often times, the area of infarction may extend to adjacent areas which are in such location that Q waves will be produced in the EKG and their presence will help enormously in making the diagnosis. Such is the case when the infarction also involves the high lateral area of the left ventricle. In this case Q waves may appear in  $L_1$  and in aVL<sup>5</sup> (Fig. 2). Since both the diaphragmatic and posterior myocardial surfaces of the left ventricle receive their blood supply from the right coronary artery, when there is thrombosis of this vessel, infarction of both areas is likely to occur.<sup>6</sup> This in turn will produce Q waves and ST segment changes in  $L_1$ ,  $L_{11}$  and aVF plus the previously described changes of "strictly posterior" myocardial infarction.

More difficulty arises in interpreting the EKG when one deals with an old or healed strictly posterior myocardial infarction. In these cases one has to differentiate this entity from right ventricular hypertrophy or an atypical case of right bundle branch block. The differentiation may be difficult indeed but it is helpful to remember that positive T waves in  $V_1$  are very rare in adults with right ventricular hypertrophy (Fig. 3). On the other hand, in the great majority of cases of direct posterior myocardial infarction, the tall R wave in  $V_1$  is followed by a positive T wave.<sup>7</sup>

There are cases of posterior myocardial infarction where the diagnosis can be made only by VCG. As we have seen, in posterior myocardial infarction the initial vector forces of the horizontal plane are increased and are predominantly forwardly oriented. In addition, the speed of inscription of these initial vectors is increased and the rotation of the QRS loop in the horizontal plane is predominantly counterclockwise. In right ventricular hypertrophy, the rotation of the QRS loop in the horizontal plane is predominantly clockwise; the initial portion of the centrifugal limb is not of greater magnitude nor is it inscribed at a faster speed. In right bundle branch block the VCG shows a terminally inscribed appendage directed anteriorly superiorly and to the right. This

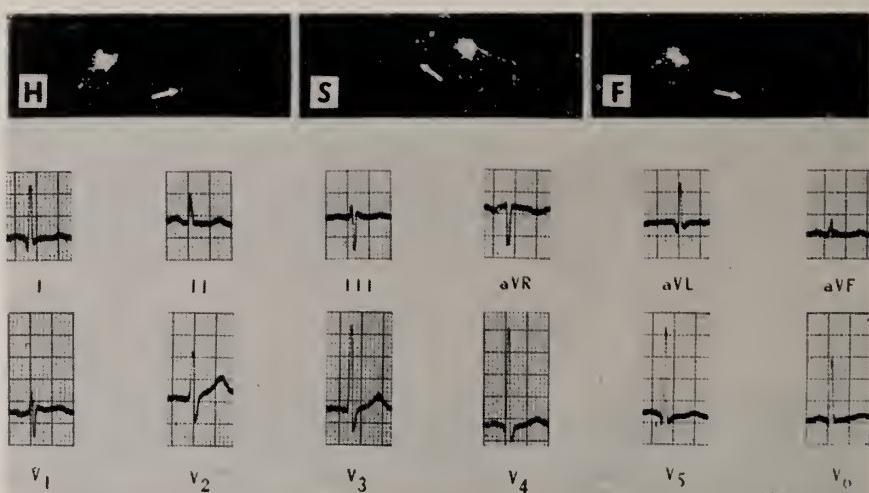


Fig. 3 — EKG shows a tall r and inversion of T wave on  $V_1$ . VCG shows right ventricular hypertrophy.

terminal appendage will show closely spaced dots as evidence of delayed conduction.

The T loop orientation in the VCG is another help in the diagnosis of posterior myocardial infarction. In this entity the T loop shows the same orientation of the initial portions of the QRS loop in all planes. In contradistinction, in right ventricular hypertrophy and right bundle branch block the T loop has a tendency to oppose the QRS loop.

#### SUMMARY

Strict posterior myocardial infarction presents a peculiar problem for diagnosis by EKG since, because of its location in the posterior wall of the left ventricle, no abnormal Q waves are seen in the EKG. The EKG pattern of this entity is difficult to distinguish from Right Ventricular Hypertrophy or Right Bundle Branch Block. The value of the VCG in the diagnosis of this type of infarction is discussed.

Strict posterior myocardial infarction is to be suspected in patients with history of coronary thrombosis and EKG findings of tall R waves in  $V_1$  with upright and even tall T waves in  $V_1-V_2$  with ST depression in the acute phase.

The VCG in the cases shows:

1—Prominent counterclockwise rotation of the initial forces in the horizontal plane with a centripetal loop that is markedly displaced anteriorly. The initial 0.02 secs. may be abnormally rapidly inscribed and displaced more anteriorly than normal.

2—The sagittal loop shows also an abnormally anteriorly oriented initial portion of the QRS loop. The frontal plane does not show any significant abnormality.

3—The T loop is oriented nearly parallel to the initial QRS forces.

4—ST vector is oriented posteriorly and to the left.

#### RESUMEN

El diagnóstico electrocardiográfico de infarto al miocardio estrictamente posterior o dorsal presenta un problema diagnóstico ya que debido a la situación anatómica de la lesión no se ven ondas Q prominentes en el electrocardiograma (EKG). Se hace difícil distinguir entre esta condición e hipertrofia ventricular derecha y bloqueo de rama derecha. El vectorcardiograma (VCG) es muy útil para hacer esta distinción.

Un infarto estrictamente posterior debe ser sospechado cuando hay historial de dolor precordial y el EKG demuestra ondas R altas en V<sub>1</sub> seguidas de ondas T positivas en V<sub>1</sub>, V<sub>2</sub> y depresión del segmento ST en la fase aguda.

El VCG en estos casos demuestra lo siguiente:

1—Rotación antihoraria del asa QRS en el plano horizontal con un marcado desplazamiento anterior de la parte terminal del asa QRS.

2—Desplazamiento anterior de la porción inicial del asa QRS en el plano sagital.

3—El asa de T está orientado paralelo a los vectores iniciales del asa QRS.

4—El vector ST está orientando hacia la izquierda y posteriormente.

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## EVALUACION CARDIOVASCULAR EN GERIATRIA\*

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### Introducción:

A pesar de los innumerables estudios e investigaciones llevados a efecto en todo el mundo civilizado en relación con la senectud, todavía no sabemos con exactitud cuál es su causa, o cuáles son sus causas.

Ni siquiera contamos con una buena y abarcadora definición del proceso. El que el envejecimiento sea "un proceso biológico causante de un aumento de susceptibilidad a la enfermedad", como lo describe Confort, está lejos de ser aplicable a todos los casos y a todas las enfermedades.

Los signos característicos del envejecimiento empiezan en la infancia. Muchas células se reproducen y nacen y otras tantas mueren todos los días.

La senectud, íntimamente ligada a la genética y al medio ambiente, es algo muy relativo. Un empleado público, un oficinista o un maestro se retira quiera que no, entre los 65 y 70 años de edad, pero un senador o un Jefe de Estado pueden seguir siéndolo a veces hasta después de los 87 años. Para un boxeador, la edad de la eficiencia y la fama está entre los 20 y los 30 años, para un tenista antes de los 35 años, en el deporte de la natación son 18 años para las mujeres y 24 para los hombres y entre los 18 y 28 para los atletas corredores.

Algunos insectos viven sólo un día, algunos reptiles viven varios cientos de años, las ratas son viejas a los 4 años, los conejillos de la India a los 8, los caballos a los 30 y las tortugas gigantes viven hasta 300 años.

La vida máxima de casi todos los mamíferos es seis veces más que el tiempo de crecimiento. El hombre generalmente crece hasta los 20 años de edad. Su vida máxima es, por lo tanto, alrededor de 120 años.

Todos deseamos vivir muchos años, pero nadie quiere envejecer. Buscando infructuosamente la fuente de la eterna juventud Ponce de León dió su vida y Fausto vendió su alma.

### El problema médico:

Las enfermedades del corazón representan actualmente en mi

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país, como en casi todos los países llamados progresistas y civilizados del mundo, la causa más frecuente de muerte. Si el progreso y la civilización han traído como consecuencia ese gran aumento en enfermedades del corazón, a la verdad que no debiéramos sentirnos orgullosos de ellos.

A pesar de todas las nuevas técnicas de laboratorio, de los adelantos en electrofisiología y de las modernas aplicaciones clínicas de la física nuclear seguimos creyendo que lo esencial en la evaluación de los problemas cardiovasculares depende hoy como ayer de un buen y completo historial clínico tomado por el propio médico y de simples y bien probados métodos de exploración física. Unos ojos que puedan mirar y ver, un par de oídos que sepan captar los sonidos, unas manos que palpen y unos dedos bien entrenados en la percusión no pueden substituirse por el más moderno equipo de rayos X, ni por el mejor calibrado electrocardiógrafo. Por muy eficaz que un computador electrónico resultara ser, nunca sería mejor que los millares de microscópicos computadores biológicos con que contamos en nuestro propio cerebro.

No se interpreten mis palabras como de menospicio al laboratorio y a los aparatos e instrumentos de precisión. Muy al contrario los tenemos y los usamos todos los días como ayuda complementaria. Pero insistimos en que debemos seguir siendo nosotros los "amos", los "dueños", los "jefes", los "señores" de esos aparatos e instrumentos y nunca sus "esclavos" y no debemos creer ciegamente en ellos como si fueran parábolas del Santo Evangelio.

Una evaluación cardiovascular completa debe incluir no sólo la exploración del sistema circulatorio en sí, sino también la función del sistema renal y del sistema respiratorio.

Nos proponemos discutir o comentar algunos de los problemas cardiovasculares con que más frecuentemente nos confrontamos en nuestra asociación y colaboración con el cirujano y con el anestesiólogo.

#### Enfermedad de la Arteria Coronaria:

El riesgo quirúrgico es mayor en las enfermedades de las arterias coronarias que en cualquier otra cardiopatía. La morbilidad y mortalidad en enfermos coronarianos sometidos a cirugía es dos a tres veces mayor que la del resto de la población quirúrgica.

En casos de insuficiencia coronaria o angina de pecho dependemos más, de la historia del paciente y de la frecuencia e intensidad del dolor en las actividades de su vida diaria que en los datos obtenidos de las pruebas de ejercicio y del electrocardiograma.

Cuando la angina de pecho ocurre con mayor frecuencia y con

menos provocación ya sea antes o después de un ataque de trombosis coronaria las intervenciones quirúrgicas deben evitarse o posponerse.

Es raro que los signos y síntomas clásicos del infarto agudo del miocardio se observen en el viejo. El cuadro es generalmente menos dramático. El dolor no es tan intenso, a veces es sólo una ligera molestia retroesternal. Aunque presentan un descenso moderado en la tensión arterial el shock casi nunca se manifiesta. El diagnóstico se establece por un aumento en la temperatura, leucocitosis discreta, aumento en las transaminasas oxaloacética y dehidrogenasa láctica y por las alteraciones características en el electrocardiograma.

Después de un ataque de trombosis coronaria no se debiera practicar ninguna intervención quirúrgica electiva hasta tres meses y preferiblemente seis meses después del ataque.

Nos dice Friedberg,<sup>1</sup> sin embargo, que el enfermo coronariano resiste cualquier intervención quirúrgica siempre que se pueda evitar la ansiedad y excitación preoperatoria, la anoxemia miocárdica y la anestesia profunda.

Thompson, Kelalis y Connolly<sup>2</sup> informaron 9 muertes en un grupo de 192 pacientes con historial previo de infarto del miocardio que sufrieron resección prostática transuretral; una mortalidad de 4.7%. Todas las muertes fueron por causas cardiovasculares. Es interesante apuntar aquí que no hubo en esa serie, relación alguna entre la mortalidad y el tiempo transcurrido entre la operación y el infarto del miocardio pero la mortalidad fue mayor en aquellos sujetos que habían sufrido poco antes otra operación de cirugía mayor.

El problema de cirugía de emergencia podría presentarse a un enfermo cardíaco que está sometido a terapia anticoagulante prolongada. Si se tratara de cirugía menor como la extracción de un diente, no importaría el tiempo de protrombina, pero si se tratara de una operación abdominal durante la cual se deberán exponer y cortar grandes vasos, la costumbre establecida, la que se siguió con el Presidente Eisenhower, consistía en administrar una dosis grande de vitamina K<sub>1</sub>, intravenosamente. En estos casos se corre siempre el peligro de que la rápida restauración del tiempo de protrombina a niveles normales pudiera cambiar en cuestión de horas un estado de hipocoagulabilidad por un estado de hipercoagulabilidad de la sangre y provocar la formación de trombos intravasculares.

Cuando la operación no es urgente es preferible limitarnos a descontinuar el uso de anticoagulantes sin administrar la Vitamina K<sub>1</sub>. Recordemos que no es necesario esperar a que el tiempo de protrombina regrese a 100% normal antes de practicar la in-

tervención quirúrgica. Todos hemos visto enfermos del hígado que han soportado operaciones de alta cirugía sin complicaciones hemorrágicas a pesar de que el tiempo de protrombina estaba ligeramente aumentado.

### Hipertensión Arterial:

Los enfermos hipertensos generalmente soportan las operaciones quirúrgicas casi tan bien como los normotensos. Me refiero a los casos no complicados de hipertensión esencial. Pero hemos visto como aún los casos graves de hipertensión maligna o acelerada, siempre que no presenten complicaciones serias renales o cerebrales, podrían soportar esplenectomías extensas con o sin adrenalectomías parciales tan de moda en los grandes centros quirúrgicos hace algunos años.

Es bien sabido que se necesita una reducción de no menos de un 60% de la función renal para que el nitrógeno uréico empiece a aumentar en la sangre. Eso quiere decir que la presencia de 25 a 30 mg. por 100 cc. de urea sérica significa de por sí una notable reducción en la función renal y que un nuevo o mayor insulto al glomérulo o al nefrón como consecuencia de trastornos electrolíticos o del shock operatorio podrían provocar una descompensación renal y llevar al paciente a un estado urémico.

No creo sea esta la oportunidad para describir las distintas pruebas de función renal que se practican hoy día en el laboratorio. Nos limitamos a mencionar entre estas las pruebas de eliminación de fenolsulfotaleína, la depuración de la urea, el renograma con hipurán radioactivo, el pielograma descendente, la prueba de Howard Rappaport, el arteriograma renal etc.

Tampoco estaría justificado el abundar en los peligros del sondeo vesical y del pielograma ascendente. Sí puedo decirles que recuerdo muy bien el día en que al presentársenos un informe urinario de una mujer, lo primero que preguntábamos era si la muestra había sido obtenida por cateterización o no. Si no había sido un espécimen cateterizado descartábamos el informe por considerarlo sin valor alguno. Hoy debo confesar que nunca o muy raras veces ordenamos cateterizar a nadie para obtener una muestra de orina ni aún para cultivo. Condenamos el uso, o mejor dicho, el abuso de la sonda o cateter como instrumento de diagnóstico.

En caso de hematuria podemos evitar investigaciones costosas y desagradables si examinamos cuidadosamente el sedimento urinario y constatamos la presencia de cilindros hemáticos. Su presencia en el sedimento descarta en la inmensa mayoría de los casos la posibilidad de lesiones o tumores en la pelvis renal, en los ureteres, la vejiga y la uretra.

Otra investigación fácil e inocua que está al alcance de todo enfermo por pobre que sea y en la cual no insistimos suficientemente los internistas y cardiólogos es la radiografía simple del abdomen. Debemos insistir en que el radiólogo nos informe el tamaño de los riñones. Esto es relativamente fácil aunque alguna que otra vez tuviera que recurrir a la laminografía. Un riñón que produzca una sombra de 13 cm. de largo y 5 cm. de ancho es casi siempre un riñón normal. Una sombra grande representa, probablemente un riñón hidronefrótico. Un riñón pequeño o contraído es un riñón nefrosclerótico. Un riñón que no se visualice ni por medio de la laminografía es probablemente un riñón poliquístico.

En todos los casos de hipertensión arterial practicamos rutinariamente el examen del fondo del ojo y determinación urinaria de las catecolaminas y serotonina.

El riesgo quirúrgico en los hipertensos aumenta en presencia de fallo cardíaco, de isquemia coronariana, de insuficiencia renal, de un previo accidente cerebral o de diabetes mellitus.

Recordemos que en personas con brazos muy gruesos la tensión arterial puede llegar hasta 40 mm. de mercurio por encima de la verdadera tensión intra-arterial y por el contrario en casos con brazos muy flacos el esfigmomanómetro puede darnos cifras 40 mm. de mercurio por debajo de la real.

En algunos enfermos hipertensos hemos encontrado muy útil el procedimiento de hacer una segunda y hasta una tercera determinación de la tensión arterial mientras el sujeto toma rápidas y profundas inspiraciones. Generalmente se obtienen cifras tensionales mucho más bajas durante ese acto sobre todo en aquellos enfermos con inestabilidad emocional.

En algunos casos de pacientes con brazos extremadamente gruesos aplicamos el brazalete del esfigmomanómetro en el antebrazo y oímos los sonidos de Korotokoff auscultando sobre la arteria radial en el mismo sitio donde acostumbramos a palpar el pulso.

Es muy importante excluir la posibilidad de un feocromocitoma en todo caso quirúrgico. Si se sabe de antemano que el paciente tiene un feocromocitoma el caso se puede manejar relativamente bien con el uso juicioso de Regitina o de Norepinefrina o Levofed durante el proceso quirúrgico, pero si no se sospecha la lesión el enfermo bajo anestesia general puede desarrollar crisis de hipertensión arterial acompañada por arritmias y seguida por shock, edema agudo del pulmón y/o accidentes cerebrovasculares.

El uso de las nuevas y efectivas drogas antihipertensivas nos ha traído también nuevos problemas relacionados con la cirugía. Pacientes hipertensos que presentan cardiomegalia y que han sufrido episodios de insuficiencia congestiva del corazón, pueden

desarrollar congestión pulmonar fulminante si se les hubieran suspendido súbitamente las drogas antipresoras durante el período pre-operatorio. Creemos por lo tanto que las drogas antipresoras potentes no deben suspenderse a ningún enfermo hipertenso ni pre ni postoperatoriamente, a menos que hayan entrado en un estado hipotensivo después de la operación.

Tanto la Guanetidina (Ismelin) como la Rauwolfia y sus derivados tienden a bajar la concentración de catecolaminas en el músculo cardíaco, en las paredes de los vasos sanguíneos, en la médula suprarenal, en los ganglios simpáticos y en el cerebro. La Guanetidina es una droga más potente que la otra y por consiguiente se usa en los casos más serios de hipertensión arterial. Esta droga se debe continuar aunque en dosis menores durante todo el curso pre y postoperatorio del paciente. En cambio *nosotros creamos* que la Rauwolfia y sus derivados Serpasil y Reserpina se deben omitir semanas antes de la operación sin que esto implique peligro de aumento considerable de la tensión arterial y para evitar las crisis hipotensivas que a veces se presentan en la sala de operaciones en pacientes que han recibido cursos prolongados de estas drogas que eliminan las catecolaminas y la serotonina del músculo cardíaco.

En casos de crisis hipotensivas durante o después del acto operatorio nosotros preferimos usar una combinación de norepinefrina (Levophed) y Metaraminol (Aramine) en proporción del 1 por 25. Esto es 4 mg. de norepinefrina y 100 mg. de metaraminol en 1000 cc. de solución salina normal.

No encontramos ni un solo caso de hipertensión maligna o acelerada en 3,726 enfermos de más de 60 años de edad estudiados por nosotros entre el 1947 y 1956.

Recordemos también el hecho interesante que mujeres de edad avanzada con tensiones arteriales más elevadas y concentración más alta de lípidos en la sangre, generalmente viven más que hombres de la misma edad.

#### Corazón Reumático:

Un paciente joven con un corazón reumático inactivo puede soportar cualquier intervención quirúrgica. La mejor prueba la tenemos en los cientos de casos que hoy día se someten a commissurotomía por estenosis mitral.

En cambio un enfermo viejo con una lesión valvular de origen reumático es generalmente un riesgo quirúrgico pobre, sencillamente porque la lesión reumática se ha complicado con una ateroesclerosis de las coronarias que no pueden en esas condiciones de estrechez de su luz llevar la cantidad de sangre necesaria a un corazón hipertrofiado.

En nuestra opinión todos los casos de estrechez mitral que hayan de ser operados se deben digitalizar profilácticamente.

Se debe sospechar corazón reumático en presencia de cardiomegalía con fibrilación, auricular, óigase o no el soplo presistólico característico de la estenosis mitral.

### Estrechez Aórtica:

La estrechez aórtica de etiología reumática en un paciente de 40 años de edad es más seria que la estrechez aórtica de origen arterioesclerótico en un paciente de 60. La muerte súbita no es rara en los enfermos con estrechez calcífica de las válvulas aórticas. Algunas de las muertes inexplicables durante la anestesia y durante operaciones de cirugía menor se han debido a estrechez aórtica insospechada. Es muy importante, por lo tanto, el descartar esa posibilidad en todo paciente quirúrgico.

Los libros de texto y nuestros antiguos maestros nos describieron los hallazgos físicos en casos de estrechez aórtica de la siguiente manera: se oye un soplo sistólico áspero y fuerte con ausencia del segundo sonido aórtico, acompañado de un tril palpable en el segundo espacio intercostal a la derecha. En el fonocardiograma el soplo aparece en forma de diamante. El tril se palpa mejor en exhalación y con el enfermo inclinado hacia adelante. Las válvulas semilunares se calcifican, el ventrículo izquierdo se hipertrofia concéntricamente y es baja la presión media. En la práctica hemos visto como los llamados signos clásicos de la estenosis aórtica están ausentes muchas más veces que presentes.

Debemos sospechar la estrechez aórtica en todo paciente que sufre de ataques de marcos o síncope, si se queja de dolor torácico parecido al de la angina de pecho pero de más larga duración o si súbitamente desarrolla edema pulmonar. A la auscultación podríamos encontrar solamente un ligero soplo en el foco aórtico, el tril puede estar ausente y frecuentemente la tensión media no es baja.

### Bloqueo de rama:

El bloqueo de rama al igual que el bloqueo cardíaco no son per se obstáculo o contraindicación para una operación quirúrgica. Esto se aplica especialmente al bloqueo de rama derecha que como sabemos se encuentra con relativa frecuencia en individuos normales, pero cuando el bloqueo es atrioventricular y se traduce en o se manifiesta como ataques de Adams-Stokes entonces sí que el riesgo quirúrgico es grande.

### Fibrilación Auricular Crónica:

La fibrilación atrial crónica en un corazón bien compensado no aumenta materialmente el riesgo quirúrgico. Encontramos complicaciones cuando el paciente fibrilador no ha sido adecuadamente digitalizado, cuando existe historia reciente de angina de pecho o de azotemia y cuando el enfermo es además enfisematoso u obeso.

En todo enfermo viejo que esté fibrilando debemos eliminar la posibilidad de un hipertiroidismo oculto preferiblemente con la prueba de la captación de iodo radioactivo, aunque el enfermo no demuestre ninguno de los signos clásicos o característicos de tirotoxicosis.

Las manos calientes en un enfermo cuyo corazón está fibrilando es un signo bastante sospechoso de tirotoxicosis. La presencia de manos frías en un enfermo con un corazón grande que esté fibrilando nos sugiere estrechez mitral.

### Fallo Cardíaco:

El fallo cardíaco congestivo es uno de los mayores riesgos quirúrgicos. Nunca se debe someter a una intervención quirúrgica a ningún enfermo que esté en descompensación cardíaca. Los viejos, sobre todo, deben ser cuidadosa y minusiosamente investigados para descubrir cualquier pequeño signo o síntoma de insuficiencia del miocardio.

No le atribuyamos siempre al cigarrillo o al efisema senil la tos persistente del viejo. Pudiera esa tos ser la manifestación inicial y quizás por algún tiempo la única evidencia clínica de fallo cardíaco. La tos nocturna puede ser el resultado de la congestión pulmonar y el insomnio en el viejo puede ser la expresión de falta de aire. Cualquier manifestación de fatiga debe considerarse seriamente y no olvidemos tampoco que los trastornos digestivos de que se quejan pueden deberse a congestión pasiva del hígado.

Antes de ser sometido a una operación quirúrgica debemos corregir el edema (secar al paciente, como se dice en inglés) y digitalizar adecuadamente todo caso de insuficiencia congestiva del corazón.

El fallo cardíaco es la causa más común del edema generalizado. Es el signo más importante de la insuficiencia ventricular derecha. A pesar de las muchas hipótesis que para explicar la génesis del edema cardíaco se han presentado durante los últimos cincuenta años, la verdad es que el problema no está aún definitivamente resuelto. Lo que nadie niega en la actualidad es el hecho de que la retención de sal juega un papel importante y que la retención de agua es secundaria a la retención de sal. Antes se creía

que el edema se debía a la transudación del plasma sanguíneo empujado fuera de los capilares por la hipertensión venosa, pero ahora sabemos que la retención de sal generalmente precede a la hipertensión venosa y que la cantidad de edema no guarda relación con el nivel de la presión venosa.

La disminución del flujo plasmático a través del riñón (de 600 ml/min. baja a 200 ml min.) trae como consecuencia una disminución en la filtración glomerular y un aumento en la reabsorción tubular de sal y agua. Aumenta el volumen plasmático y nos encontramos en el fallo cardíaco porque las arterias llevan poca sangre y las venas se encuentran ingurgitadas por exceso de sangre.

Pero el mecanismo fisiopatológico no es tan fácil como eso. Hay que contar también con otros factores osmóticos, oncóticos e hidrostáticos al igual que con factores hormonales entre los cuales se destaca la aldosterona. La aldosterona, que juega un papel importante en diuresis y en la reabsorción tubular de sal y agua se encuentra frecuentemente aumentada en la insuficiencia congestiva del corazón, pero a niveles mucho más bajos que en casos de nefrosis, de cirrosis del hígado, del síndrome de Conn, y del embarazo.

En cuanto al uso de la digital preferimos la administración oral de la droga y limitamos su uso intravenoso a los casos de fallo agudo que ocurrán en la sala de operaciones o como consecuencia de un infarto del miocardio y a casos de fibrilación auricular con muy rápida frecuencia ventricular.

Los casos de insuficiencia congestiva del corazón que no ceden al tratamiento clásico de restricción de sodio, diuréticos y digital deben ser cuidadosa, crítica y sistemáticamente revisados y reevaluados. Se deben descartar posibles factores complicantes tales como infecciones intercurrentes, embolias o infartos pulmonares, anemia, infarto silencioso del miocardio etc. La persistencia de la insuficiencia cardíaca se puede deber tanto a dosis insuficientes de digital como a la administración de dosis excesivas. En ese último caso el fallo cardíaco sería de origen iatrogénico.

En la práctica siempre quedarán algunos casos de descompensación cardíaca que no responden a la digital. Entre ellos mencionaremos la amiloidosis primaria, la sarcoidosis, la hipertrofia idiopática del corazón, la fibroelastosis subendocárdica, el mixoma auricular y la enfermedad de Chagas.

#### El Uso Profiláctico de la Digital:

El uso profiláctico de la digital ha sido, hasta hace poco, un campo controversial. Estudios clínicos y experimentales han com-

probado que no es cierto como se creía, que la droga produce un efecto nocivo paradójico sobre el corazón normal. Se ha comprobado sin dejar lugar a dudas que la digital aumenta la fuerza contráctil del músculo cardíaco normal y también la del corazón hipertrofiado esté o no en fallo.

El efecto farmacológico de la digital es múltiple. Posee un efecto directo inotrópico o muscular, otro efecto domotrópico que afecta la velocidad de inducción de las fibras nerviosas y una acción cronotrópica que retarda el marcapaso sinusal. La droga además tiene efectos veno y arteriopresores.

Nosotros actualmente administramos digital profilácticamente a todos los casos de estenosis mitral, a todo paciente que presente una historia de pobre reserva cardíaca o de haber alguna vez manifestado insuficiencia congestiva especialmente si pasa de los 50 años de edad, a aquellos sujetos con un corazón grande y a todo enfermo de edad avanzada cuyo electrocardiograma demuestre cambios sugestivos de isquemia coronaria o de enfermedad del miocardio.

#### **El Potasio en Toxicidad Digitálica:**

Durante los últimos años hemos estado usando distintas sales de potasio para contrarrestar las arritmias y otros efectos tóxicos de la digital. En dosis no tóxicas la digital actúa sobre la conducción a través de su acción sobre el vago, pero en dosis grandes y tóxicas la digital actúa directamente sobre el tejido especializado atrioventricular. En el primer caso, cuando la dosis no ha sido muy grande y cuando las manifestaciones tóxicas se manifiestan sólo como contracciones prematuras o bigeminismo el potasio mejora la conducción, pero cuando la intoxicación digital ha sido profunda, las sales de potasio tienden a provocar un más alto grado de bloqueo. Eso quiere decir que no podemos usar el potasio como si fuera una panacea en el tratamiento de todas las arritmias digitálicas y que su uso puede ser contraproducente en los casos de intoxicación grave.

#### **Corazón de Beriberi:**

Se debe sospechar el beriberi cuando vemos un paciente en fallo cardíaco que nos da una historia de alcoholismo crónico y de mala nutrición y cuyo corazón no presenta lesión valvular alguna. Su piel está generalmente caliente, el corazón derecho agrandado y existen signos y síntomas de neuritis periférica. El pulso es hiperquinético y rápido y alta la tensión media. Al contrario de lo que ocurre en otros casos de insuficiencia cardíaca congestiva en-

contramos en beriberi un tiempo de circulación acortado. La rápida respuesta a la administración de tiamina confirma el diagnóstico.

• • • •

### Cor Pulmonale:

No creemos que sea necesario un gran laboratorio cardiopulmonar para decidir; en los viejos, la capacidad funcional de los pulmones antes de ser sometidos a una intervención quirúrgica. Nosotros nos conformamos con el historial clínico, el examen físico rutinario, el electrocardiograma y la determinación de la capacidad vital en dos segundos y el "maximum expiratory flow rate". Con estas pruebas sencillas que practicamos en nuestra propia oficina con un pequeño aparato de fuelle llamado Vilator, de McKesson Appliances Co., podemos en la mayoría de los casos determinar si el enfermo tiene o no enfisema pulmonar.

Las alteraciones electrocardiográficas del corazón pulmonar fueron muy bien descritas en el año 1946 por los mexicanos Salazar-Mallen y Sodi-Pollares<sup>3</sup> pero la llamada P pulmonale había sido ya descrita en el 1935 por el alemán Winternitz.

La P picuda de cor pulmonale es más prominente en las derivaciones 2 y 3 en contraste con la P ancha de la estenosis mitral que se destaca en las derivaciones 1 y 2.

En el cor pulmonale pueden aparecer ondas Q prominentes en derivaciones 2, 3 y VF que podrían fácilmente confundirse con el trazo del infarto posterior o diafragmático, excepto por el hecho de que las ondas T aparecen en desnivel negativo en el infarto y en desnivel positivo en el cor pulmonale.

Para nosotros los cambios más obvios en casos de enfermedad pulmonar sobre todo en enfisema pulmonar son la verticalización del eje medio de la onda P y la presencia de una onda P netamente invertida en VL.

En un estudio practicado por nosotros en 322 pacientes de 80 o más años de edad, encontramos evidencias electrocardiográficas de hipertrofia ventricular izquierda en 16%, pero evidencias de hipertrofia o de sobrecarga ventricular derecha estuvieron ausentes o fueron mínimas. Ese estudio nos llevó a la conclusión de que los casos típicos o clásicos de cor pulmonale raras veces llegan a los ochenta años de edad.

### Anestesia:

Durante el pasado año estudiamos los electrocardiogramas pre y postanestésicos en 100 casos consecutivos admitidos al hospital para tratamiento quirúrgico. Las edades oscilaban entre 4 y

87 años. Hubo 7 pacientes en el grupo entre 4 y 20 años de edad, 22 en el grupo de 21 a 40 años, 30 en el grupo de 41 y 60 años y 41 casos en el grupo entre los 61 y 87 años de edad. En este último grupo tuvimos 7 octogenarios.

La mayor parte de las operaciones se practicaron bajo anestesia general que consistió de Pentotal intravenosa, óxido nitroso, eter, succinyl glucosado como relajador muscular, demerol, oxígeno etc., pero nunca se usó ni ciclopropano ni fluotano.

Algunos casos se operaron bajo anestesia intrarraquídea usando pontocaína hiperbárica en solución glucosada al 10%.

Nos decidimos a llevar a efecto ese estudio por dos razones: primero porque algunos autores han recomendado el electrocardiograma postanestésico como procedimiento de rutina en todos los casos de cirugía y segundo porque Dennis<sup>4</sup> y sus colaboradores del Cardiovascular Research Center de la Escuela de Medicina de la Universidad de Baylor informaron ocho pacientes que habían desarrollado ondas T profundamente invertidas durante el período inmediatamente después de la operación o de la anestesia.

En todos los casos usaron Pentotal como agente preanestésico y luego succinilcolina, D-tubocurare, anectina o fluotano. Todos los pacientes menos uno pasaron por un período de hipotensión antes de administrárseles drogas vasopresoras (neosinefrina, aramina o Levofed). En cuatro pacientes la hipotensión se desarrolló después de un ataque agudo y fulminante de edema pulmonar. Esos autores se inclinaban a acusar al Pentotal, dejando en libertad a todas las otras drogas y agentes anestésicos usados durante el proceso operatorio.

Los cambios observados por nosotros fueron mínimos y de corta duración y aunque se limitaron a la onda T en la mayoría de los casos, las ondas T profundamente invertidas descritas por los investigadores de Texas no aparecieron en ninguno de nuestros enfermos.

Llegamos a la conclusión de que no se justifica el hacer electrocardiograma post-operatorio como procedimiento de rutina, pero si creemos que el electrocardiograma preoperatorio está indicado en todo caso quirúrgico.

El electrocardiograma postanestésico o postoperatorio se puede limitar a aquellos pacientes que durante o poco después de la operación presentan una marcada bradicardia o arritmia, una súbita e inexplicable taquicardia, hipoxia o hipotensión que no ceden a la restauración del volumen circulante.

Nuestros estudios confirmaron el bien conocido hecho que un trazado electrocardiográfico por anormal que parezca no es *per se* obstáculo para una intervención quirúrgica necesaria.

### "Status" Mental

Un octogenario vigoroso y optimista es mucho mejor riesgo quirúrgico que un paciente más joven pero débil y pesimista.

Todos hemos visto el viejo con o sin enfermedad cardíaca que se siente aburrido, amargado, frustrado, solitario e inútil. Estos enfermos presentan depresión mental y deterioro físico. En su desesperación y desconsuelo no es raro que busquen la solución en el suicidio. Insisten en que "se les deje morir en paz". Pero paz es lo que necesita su mente, su cuerpo y su alma. Paz que ni las drogas ataráxicas ni las excitantes pueden proporcionarles, pero que la consigue el médico, no el buen médico, sino el médico bueno con su paciencia, su interés, su simpatía y su caridad. A estos enfermos yo les receto una sonrisa cada 3 horas y les digo que "la sonrisa es un atributo que Dios le dió al hombre y negó a los animales."

Si yo fuera cirujano no operaría a ninguno de estos enfermos hasta que hayan aprendido de nuevo a sonreír.

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## ACCURACY OF DEATH CERTIFICATION IN METROPOLITAN SAN JUAN\*

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Filling out a death certificate usually constitutes something of a problem to the average physician. Though the frequency with which he faces this problem depends on his type of practice, the doctor is generally concerned with two things: having the correct diagnosis and making it fit into the death certificate. Although the first problem is undoubtedly the more important, it is the second which more frequently causes greater trouble.

To begin with, the International Form of Medical Certificate of Cause of Death, which is the one used in Puerto Rico (Fig. 1), although apparently simple and straightforward enough for coding and statistical purposes, leaves much to be desired when clinical information is to be emptied into it. The form calls for a single cause of death; yet, as any physician knows, it is not unusual for two or three serious diseases to be present and to contribute equally to a patient's demise; or it may be impossible for the physician to determine which of several conditions present was actually responsible for the decease.

It happens occasionally that the physician is called upon to make a decision in the middle of the night or during busy hours, by relatives or funeral directors in a hurry to dispose of the body, so that insufficient time is available for the certifying doctor to exercise his best judgment in pinpointing the cause of death. In many occasions he depends entirely on sketchy information given by relatives, as he has never cared for the deceased.

Another source of difficulty arises from the fact that the cause of death stated by the physician is coded by a clerk who has no knowledge of medicine and who is guided by a set of rules which at times are quite arbitrary.<sup>1</sup> Theoretically, if the certificate has been correctly filled out, the last diagnosis written in part I of the form will be coded, but this is not always so. Nevertheless the diagnosis coded is used to prepare statistical tables of causes of death in Puerto Rico.<sup>2</sup>

During the six-month period from May 1, 1963, through October 31, 1963, a study of all deaths between the ages of 20 to 64 years occurring in the residents of the San Juan Metropolitan

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CERTIFICACION MEDICA		Intervalo entre su Comienzo y el Fallecimiento
I. Enfermedad o Causa Inmediata que produjo la muerte CAUSAS ANTECEDENTES.	(a)	
Condiciones patológicas que condujeron a la causa directa de muerte anotada en el apartado (a) indicando la causa fundamental en último término.	Debido (b)	
Causa de la muerte no significa la forma de morir como colapso cardíaco, astenia, etc. Significa la enfermedad, lesión o complicación que ocasionó la muerte.		Debido (c)
II. Otras Condiciones de Importancia:		
Condiciones que contribuyeron a la muerte pero que no estaban relacionadas con la enfermedad que causó la muerte		

FIGURE 1

Area was carried out. One of the purposes of the study was to find out how much medical information was available in each case that would justify the diagnosis entered as cause of death in the death certificate. A diagnosis was made on the basis of this information and compared with the diagnosis on the certificate. Of the 674 certificates of all deaths for the study period there were 184 instances in which a different diagnosis was made. This paper presents an analysis of these cases.

#### MATERIALS AND METHODS

For the purposes of this study the San Juan Metropolitan Area was considered to include San Juan-Santurce, Río Piedras, Bayamón, Carolina, Cataño and Guaynabo. The actual procedure followed is described in detail elsewhere.<sup>3</sup> Medical information on all death cases was obtained from one of four possible sources: autopsy protocols, hospital records, attending physicians, or relatives of the deceased, listed here in what was considered descending order of reliability. In autopsy cases the cause of death given in the protocol was considered to be correct, based on the most reliable information obtainable. In cases without autopsy, the information was evaluated independently by two reviewers, each of which wrote a new death diagnosis for each case. A reviewing committee then established the final diagnosis for each death, settling any disagreements between the reviewers. The committee also decided the degree of certainty with which each diagnosis had been made. "Almost certain" was the highest degree of certainty and corresponded in general to diagnoses based on autopsy findings or biopsy studies. "Reasonably sure" was used for diagnoses based on fairly well established clinical pictures and laboratory findings. The category "doubtful" was applied to diagnoses supported by incomplete or inconclusive data. When the information was insufficient to reach any diagnosis, the case was labeled "unable to diagnose".

The final death diagnosis for each case was then coded by the regular clerks of the Department of Health who code all death certificates; and the original and the new codes were compared. Usually a four-digit code is entered, but since the last digit indicates only a refinement of the diagnosis, in this study only the first three digits of each code were compared to determine whether there had been a change in the diagnosis or not.

In the International Classification of Diseases<sup>1</sup> diagnoses are listed under 17 sections. Each section consists of a broad group of diseases, or of diseases of an organ system, and usually contains a number of subsections under each of which there is listed

a number of diagnoses. In general, then, a change in diagnosis within a subsection is probably minor, one involving a change of subsection is probably greater, while one which involves a change of section is probably a major change. It hardly seems worth mentioning that whenever reference is made to a "change in diagnosis", such change was entered in the study records only, and not, of course, in the original death certificates, which were left intact.

#### RESULTS

The over-all results of the entire study are presented elsewhere.<sup>3</sup>

Of the 674 death certificates reviewed, changes in the 3-digit code were made in 184, or about 27% of the cases, an appalling figure until one considers the nature of the changes.

Table I compares the place of death for the 184 cases in which a change in diagnosis was made to 490 deaths in which there was no change. In both groups over half the cases had died in a hospital. Changes in diagnosis were made in 72 (34%) of 214 deaths in the home, in 98 (27%) of 363 deaths in the hospital, and in 14 (14%) of 97 deaths in other places.

TABLE I  
PLACE OF DEATH OF CASES WITH CHANGE IN CAUSE OF DEATH  
COMPARED WITH CASES WITH NO CHANGE

Place of Death	Cases with change	Cases with no change	Total
Home	72	142	214
Hospital	98	265	363
Other	14	83	97
TOTAL	184	490	674

Table II presents a comparison of the group with change in diagnosis to the group with no change, with respect to the principal source of data on which the new evaluation was made. Of the cases with change, over 1/3 had revised diagnoses based on autopsy protocols, while in almost half, the information was obtained from hospital records. These proportions were roughly inverted in the cases with no change. Of 355 deaths in which an autopsy was the source of data 67 (19%) had a change in diagnosis, of 237 based on hospital record information 81 (34%), of 46 diagnosed from information given by the certifying physician 19 (41%), and of 36 based on data given by relatives 17 (47%).

TABLE II  
MAIN SOURCE OF DATA OF CASES WITH CHANGE IN CAUSE OF DEATH COMPARED WITH CASES WITH NO CHANGE

Source of Data	Cases with change	Cases with no change	Total
Autopsy	67	288	355
Hospital record	81	156	237
Certifying physician	19	27	46
Relatives of deceased	17	19	36
TOTAL	184	490	674

Table III shows the certainty with which the diagnosis was made by the reviewers in the group of cases with change compared to those without change. Among the former group the reviewers were almost certain in over half the cases and reasonably sure in an additional fourth; in the group with no change 95% of the cases fell into these same two categories. Of the cases in which the reviewer was almost certain of the diagnosis 23% had a change, of those classified as reasonably sure 31%, of those diagnosed as doubtful 48%, and of the cases which could not be diagnosed 67% were changes.

TABLE III  
REVIEWER'S CERTAINTY OF DIAGNOSIS IN CASES WITH CHANGE IN CAUSE OF DEATH COMPARED WITH CASES WITH NO CHANGE

Degree of Certainty	Cases with change		Cases with no change	
	No.	%	No.	%
Almost certain	103	56	352	72
Reasonably sure	52	28	115	24
Doubtful	15	8	16	3
Unable to diagnose	14	8	7	1
TOTAL	184	100	490	100

Analysis of the magnitude of the change in diagnosis in the 184 cases showed that 101 cases registered a change of section, 35 a change of subsection, and 48 a change within subsection. The degree of change occurring within a subsection is exemplified by these actual instances: cerebral hemorrhage changed to subarachnoid hemorrhage, cancer of the rectum changed to cancer of the colon, motor vehicle accident involving pedestrian changed to motor vehicle accident including two cars. Examples of the changes in diagnosis involving a change of subsection are as follows: arteriosclerotic heart disease changed to hypertensive heart disease,

TABLE IV — ANALYSIS OF 13 CASES WHICH REVIEWER WAS UNABLE  
TO DIAGNOSE WITH THE BEST AVAILABLE DATA

No.	Study No.	Diagnosis on Death Certificate	Place of Death	Source of Data	Remarks
1	2028	Cirrhosis of liver	Home	Relatives	Incomplete information given by relatives.
2	3003	Peptic ulcer	Home	Relatives	Incomplete information given by relatives.
3	5222	Cerebral hemorrhage	Home	Relatives	Incomplete information given by relatives.
4	6234	Cerebral thrombosis	Home	Relatives	Incomplete information given by relatives.
5	1044	Diabetes mellitus	Home	Physician	Dead on arrival.
6	6038	Diabetes mellitus	Home	Relatives	Seen in terminal state by physician.
7	2020	Cerebrovascular accident	Home	Physician	Vague symptomatology.
8	6064	Generalized arteriosclerosis	Home	Physician	Vague symptomatology. Seen once by physician.
9	6225	Cerebral thrombosis	Home	Hospital record	Vague symptomatology. Seen only once by certifying physician.
10	6103	Liver disease	Hospital	Hospital record	Available data insufficient for diagnosis of cause of death.
11	2006	Cirrhosis of liver	Hospital	Hospital record	Record incomplete.
12	1087	Malnutrition	Home	Hospital record	Psychiatric case with obscure history.
13	1035	Gun shot wound	Other	Autopsy protocol not available	No record obtainable in two hospitals visited. Certifying physician could not be localized. Relatives' address not available.

TABLE V — ANALYSIS OF 8 CASES WITH NO APPARENT EXPLANATION FOR  
THE CHANGE IN WHICH THE REVISED DIAGNOSIS WAS DOUBTFUL

No.	Study No.	Initial Diagnosis Coded As	Revised Diagnosis Coded As	Place of Death	Source of Data	Remarks
1	1093	Undiagnosed disease	Arteriosclerotic heart disease	Hospital	Relatives	Sudden death.
2	5141	Cerebral hemorrhage	Arteriosclerotic heart disease	Home	Relatives	Sudden death.
3	5124	Anemia	Nephrosis	Hospital	Hospital record	Psychiatric patient.
4	2022	Dengue	Unspecified gastrointestinal disease	Hospital	Relatives	Died within 2 hours of hospitalization.
5	1037	Arteriosclerotic heart disease	Gallbladder disease	Hospital	Hospital record	Died following gall bladder surgery.
6	6001	Liver cirrhosis	Pulmonary tuberculosis	Home	Relatives	Diagnosis established previously at T B Hospital.
7	6045	Unspecified carcinomatosis	Liver cirrhosis	Home	Physician	
8	6181	Arteriosclerotic heart disease	Nephritis	Hospital	Hospital record	

cancer of the esophagus changed to cancer of the tongue, rheumatic fever changed to rheumatic heart disease.

Analysis of the 101 cases in which a change of section was effected showed that in 24 the change consisted of an inversion of the order in which two diagnoses had been entered in the death certificate before and after review; in 25 the original diagnosis made on the basis of gross autopsy findings had been changed to a new one following microscopic examination of the tissues; three cases labeled "coder's choice" had exactly the same list of diagnoses before and after review, but the coder chose a different diagnosis from the list on each occasion; in 13 instances the available information was judged to be insufficient for arriving at a diagnosis; while in 36 cases no explanation for the change in diagnosis could be made; i.e., the changes were real rather than apparent. In this latter group the revised diagnosis was considered to be almost certain in 11, reasonably sure in 17, and doubtful in 8.

The 13 cases considered to have insufficient data for establishing a diagnosis are analyzed individually in Table IV. Table V shows an analysis of the 8 cases in which the reviewer was doubtful of the diagnosis. The 17 cases in which the reviewer was reasonably sure of the diagnosis are presented in Table VI. The diagnosis change in many of these was not as drastic as could be expected. Table VII analyzes the 11 deaths in which the reviewer was almost certain of the revised diagnosis. Practically all these cases had virtually incontrovertible evidence of the respective diagnosis: 3 were diagnosed by biopsy, one by bacteriological tests, one by thorough laboratory work-up, 5 had classical to recognizable clinical syndromes, and one a congenital condition.

From the results above it seems that significant changes in diagnosis were made in the 13 cases which the reviewers were unable to diagnose and in the 36 cases in which the change in diagnosis involved a change of code section. These 49 cases represent just over 7% of the total 674 certificates studied, a much more reasonable figure than the 27% presented initially. If from these one subtracts 10 cases in which the change in diagnosis was not significant from a clinical point of view, it turns out that a major change was made in less than 6% of the total.

#### COMMENTS

The results suggest that probably the only factor which might help to increase the accuracy of diagnoses on death certificates is exerting a maximum effort to obtain the best clinical data available in each case. Even so, such exertion could be expected to result in only a 6 to 7% improvement in accuracy. Whether it is

TABLE VI — ANALYSIS OF 17 CASES WITH NO APPARENT EXPLANATION FOR THE CHANGE IN WHICH THE REVISED DIAGNOSIS WAS REASONABLY SURE

No.	Study No.	Initial Diagnosis Coded As	Revised Diagnosis Coded As	Place of Death	Source of Data
1	6042	Heart failure	Arteriosclerotic heart disease <sup>1</sup>	Home	Hospital record
2	6012	Heart failure	Arteriosclerotic heart disease <sup>2</sup>	Home	Hospital record
3	6167	Heart failure	Unspecified heart disease	Home	Hospital record
4	5183	Undiagnosed disease	Liver disease <sup>3</sup>	Hospital	Hospital record
5	5127	Generalized arteriosclerosis	Accidental fall	Hospital	Hospital record
6	6105	Essential hypertension	Heart failure	Hospital	Hospital record
7	6078	Liver disease	Chronic alcoholism	Hospital	Hospital record
8	6209	Cerebral embolus	Hypertensive heart disease	Hospital	Physician
9	6150	Cerebral hemorrhage	Chronic pyelonephritis	Home	Hospital record
10	8037	CO <sub>2</sub> narcosis	Arteriosclerotic heart disease	Hospital	Hospital record
11	5005	Chronic pulmonary disease	Respiratory failure	Home	Physician
12	6096	Pneumonia	Pulmonary tuberculosis	Home	Hospital record
13	1076	Cancer of stomach	Liver cirrhosis	Home	Physician
14	5209	Pneumonia	Unspecified heart disease	Home	Hospital record
15	6061	Hypertensive heart disease	Pneumonia	Hospital	Hospital record
16	6107	Intestinal obstruction	Malignancy of unspecified site	Hospital	Hospital record
17	6146	Pneumonia	Encephalitis	Home	Physician

<sup>1</sup> Sudden death.

<sup>2</sup> Myocardial infarction by EKG.

<sup>3</sup> Died in hepatic coma.

TABLE VII — ANALYSIS OF 11 CASES WITH NO APPARENT EXPLANATION  
FOR THE CHANGE IN WHICH THE REVISED DIAGNOSIS WAS  
ALMOST CERTAIN

No.	Study No.	Initial Diagnosis Coded As	Revised Diagnosis Coded As	Place of Death	Source of Data	Care by Certifying Physician	Remarks
1	2002	Cerebrovascular accident	Malignancy	Home	Hospital record	0	Diagnosed by biopsy.
2	6013	Generalized arteriosclerosis	Pulmonary tuberculosis	Home	Hospital record	0	Sputum positive.
3	8045	Unspecified heart disease	Weil's disease	Hospital	Hospital record	0	Classical clinical picture.
4	3009	Gastroenteritis	Sheehan's syndrome	Other	Hospital record	Less than 1 day	Diagnosed by exhaustive work np.
5	6019	Diabetes mellitus	Hypertensive heart disease	Hospital	Hospital record	Less than 1 day	Since birth. Aspirated.
6	3002	Influenza	Convulsive disorder	Home	Relatives	1 day	
7	5071	Menstrual disorder	Transfusion reaction	Hospital	Hospital record	1 day	Classical history.
8	6003	Pulmonary tuberculosis	Carcinoma of lung	Home	Hospital record	Uncertain	Diagnosed by biopsy.
9	5104	Cerebrovascular accident	Liver cirrhosis	Hospital	Hospital record	5 weeks	Died in hepatic coma.
10	5363	Carcinoma of liver	Liver cirrhosis	Home	Hospital record	1 month	Diagnosed by biopsy.
11	7007	Pneumonia	Ecclampsia	Hospital	Hospital record	8 days	Aspirated during convulsion.

practical to go to the extra trouble in every case and whether the small returns justify the extra expenditure of time and effort are points for discussion.

Diagnostic accuracy, as measured by the relative proportion of cases requiring change, varies with the place where death occurs. It is lowest for cases dying at home and highest for those dying in miscellaneous places. These relative levels of accuracy are partly explained by the fact that the certifying physician is frequently not in possession of all medical data for cases dying in the home, since most of them have been hospitalized at one time or another during the course of their illness; and that persons dying in miscellaneous places usually have autopsies, which carry a great accuracy of diagnosis.

The less reliable the source of information, the greater the proportion of cases with change in diagnosis. Autopsy cases had the least proportion of changes because the certifying physician was usually the pathologist who performed the autopsy, and changes were registered only when the microscopic examination was at variance with the gross findings. Information from hospital records, which are in general pretty reliable, led to changes in diagnosis more frequently. It was obvious that in many cases the hospital record had not been available to the certifying physician. There were not enough cases diagnosed from information given by the physician or by the relatives to evaluate these sources fairly.

The reviewers were somewhat less certain of their diagnoses in the deaths which registered changes, suggesting that these cases were probably more difficult to diagnose, even with the best medical data available. It should be emphasized that the reviewers were not aware that they were changing a diagnosis until after their own diagnostic decision had been made.

Although the majority of changes made were significant ones, most of them were due to reasons other than medical and thus beyond the control of the certifying physician.

Those cases with real changes in diagnosis are divided into four almost equal groups according to the degree of certainty of the reviewers. The group which could not be diagnosed usually presented very sketchy and incomplete information. Of course, in the majority of cases the certifying physician had one incalculable advantage over the reviewers of this study: actual observation of the patient. Naturally this also holds true for the other three groups, but in these cases the reviewers had more objective evidence to go on for making a diagnosis.

Particularly interesting is the group in which the reviewer was almost certain of the diagnosis. In most of these cases the

certifying physician either had not seen the patient or had cared for him for a very short period of time, insufficient for adequate diagnostic studies to be done. There were only 4 cases in which an accurate diagnosis could perhaps have been made after a more thorough evaluation of the available medical data.

#### CONCLUSIONS

The diagnoses of the cause of death in certificates of people aged 20 to 64 years in the San Juan Metropolitan Area have a high degree of accuracy. A painstaking effort to increase this by a thorough search for all available medical data could be expected to raise accuracy by 6 to 7% only.

As far as the accuracy of mortality statistics, this could most easily be increased by having the physician write just one diagnosis as cause of death in the certificate. In this way he could be sure that the diagnosis coded would be the one he really intended as cause of death.

#### SUMMARY

A study of 674 death certificates representing all deaths in the 20 to 64 year age groups during a six-month period in the San Juan Metropolitan Area was carried out.

An analysis is presented of 184 deaths in which a diagnosis different from the one entered in the death certificate was made by a committee of reviewers who had the best clinical data available for each case. No change in diagnosis was made in the 490 other death certificates similarly studied.

The majority of the changes were of a significant nature. However, most of them were artefacts due to inadequacies of the death certificate form and the method of coding. Very few cases were found in which the death certificate diagnosis could have been made more accurate without undue effort.

Implications of these results for physicians filling out death certificates and for mortality statistics are briefly discussed.

#### RESUMEN

Se llevó a cabo un estudio de 674 certificados de defunción que representan todas las muertes en las edades de 20 a 64 años en el Área Metropolitana de San Juan durante un período de 6 meses.

Se presenta un análisis de 184 certificados en los que un comité revisador, disponiendo de la mejor información clínica de cada

caso, diagnosticó una enfermedad distinta de la que aparecía en el certificado. En los 490 otros certificados no hubo cambio en el diagnóstico.

La mayoría de las discrepancias en el diagnóstico fueron significativas, pero las más importantes se debieron a la forma de escribir los diagnósticos en el certificado y a la manera de seleccionar uno de estos diagnósticos para codificarlo. En muy pocos casos se hubiera podido hacer un diagnóstico más preciso sin un esfuerzo desproporcionado.

Se hacen breves comentarios sobre la manera de llenar los certificados y sobre la precisión de las estadísticas de mortalidad locales.

#### Acknowledgements:

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## EPILEPTIC LAUGHTER\*

LUIS P. SANCHEZ LONGO\*\* and ANDRES OLIVER ROSE\*\*\*

Forced laughter occurring in a patient without an external precipitant is a well recognized sign of organic brain damage. It is seen in pseudobulbar palsy, cerebral arteriosclerosis, disseminated sclerosis and in amyotrophic lateral sclerosis. Prefrontal lobotomies and diencephalic lesions may also be responsible for uncontrollable outbursts of laughter.<sup>1-5</sup>

An epidemic of laughing in the Bukoba District of Tanganyika was reported in May 1963.<sup>6</sup> Two hundred and seventeen persons were attacked in two months. The illness affected 95 of 159 pupils at a girl's school. In these patients, the attacks of laughter would begin suddenly and would last from a few minutes to a few hours. The episodes were associated with restlessness, pupillary dilatation and frequently by exaggeration of the deep tendon reflexes. After the school was closed, the disease spread to a village 55 miles west of Bukoba. The laboratory studies in these cases, including spinal fluid tests and viral studies, were negative. The authors postulated mass hysteria as the most likely explanation; however, there is a belief that the condition was contagious.

Epilepsy as a causative factor in disorders of laughter is less recognized in spite of the fact that cases have been reported as early as 1898.<sup>5</sup> In cases of epileptic laughter the fit of laughter is unprovoked, involuntary, comes as a surprise and causes embarrassment to the patient. It differs from hysterical laughter in that it is of brief duration and the spell has a sudden and spontaneous ending. In doubtful cases the electroencephalographic findings and the response to anticonvulsant therapy will provide the evidence in favor of the organic etiology of the spell. Besides this, it is a compulsive reaction differing from normal laughter in that it occurs without an external precipitating cause and has no contagious quality. Epileptic laughter has been described essentially in three types of disorders: in massive myoclonic spasms, in psychomotor automatisms and in patients with lesions of the diencephalon.

The purpose of this presentation is to report three cases, two with epileptic laughter associated with massive (myoclonic) spasms and one case with psychomotor seizures.

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## CASE REPORTS

**Case No. 1.** S. C. F. is a 9 year old colored male who was first seen by us in 1959 when he was 4 years old. The child was born prematurely at the Rio Piedras Municipal Hospital weighing only 4 lbs. He suffered cyanosis at birth requiring oxygen therapy and a blood transfusion. The child was kept in an incubator for 6 weeks. At the age of 1-1/2 the child began suffering from massive tonic spasms and grand mal seizures. At the age of 3 the child developed paroxysmal compulsive laughter associated with massive myoclonic spasms or preceding grand mal seizures. Following the seizures the patient often fell asleep or remained in a prolonged post-ictal state of confusion. He began ambulating after age 2, and about that age the mother noticed spasticity of the legs with dragging of the right one, conditions that have persisted since then. Since the age of 4 the patient has gradually developed rapid enlargement of the genitalia and growth of pubic hair. The family describes peculiar episodes of uncontrollable and unexplained affectivity in which the patient becomes excessively affectionate toward strange people wanting to embrace or kiss them. These episodes are unrelated in time to the attacks of laughter.

The family history in this case is non contributory. The past medical history reveals only ascariasis at age 3, and chicken pox at the age of 1.

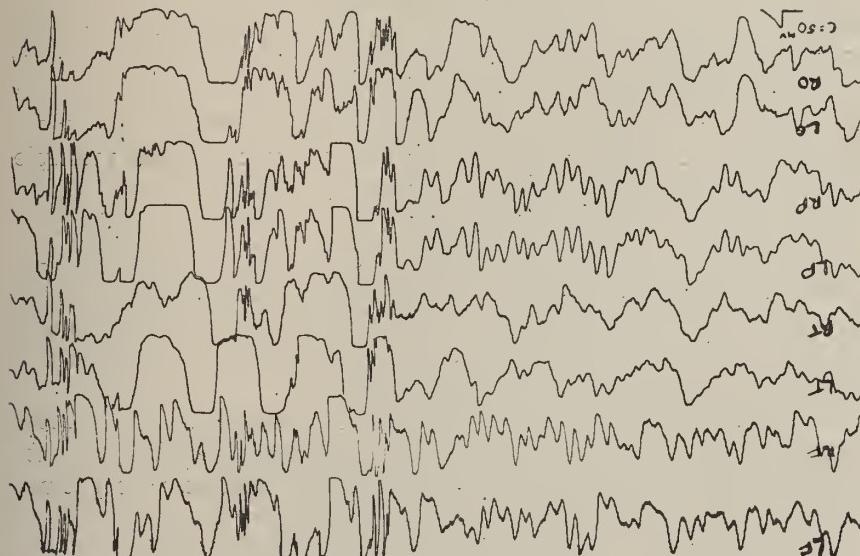


Figure 1.—This is a portion of an electroencephalogram performed at 4 years of age, in case #1. Note the abnormal epileptiform discharges consisting of multiple spikes followed by slow waves.

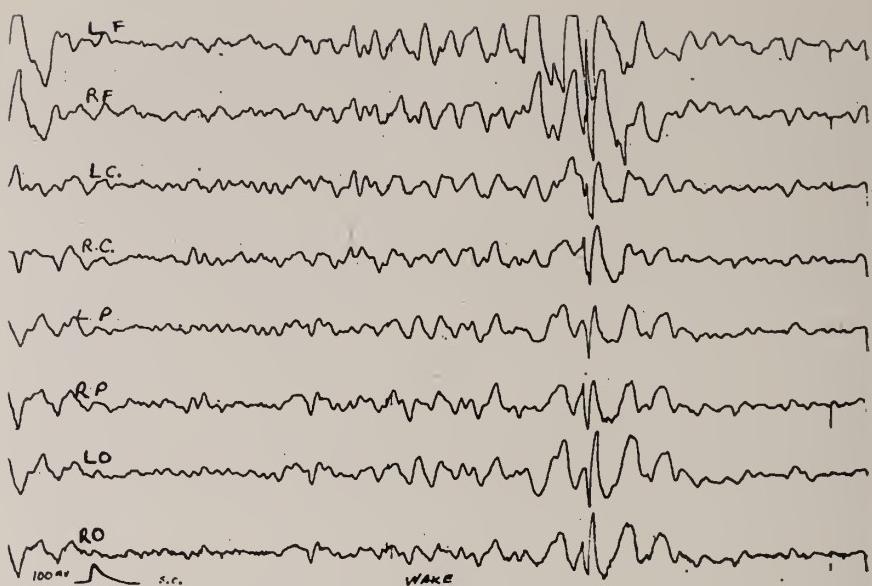


Figure 2.—This is a portion of an electroencephalogram done in patient # 1 at 9 years of age. Please note the slow waves and spikes discharges.

The general physical examination reveals a child with abnormally large male genitalia and prominent secondary sex characteristics. Repeated neurological examinations reveal moderate to severe evidence of mental retardation, increased muscle tone in the lower extremities with spasticity, and slight dragging of the right leg on ambulation.

Routine laboratory studies, blood chemistries, chest plate and skull series are negative. The electroencephalograms are characterized by abnormal paroxysmal burst of synchronized multiple spikes followed by slow waves as seen in myoclonic or centrencephalic epilepsy (see figures 1 and 2).

The patient was placed on 100 mgm. of diphenylhydantoin twice a day and on 32 mgms. of phenobarbital three times per day. With this treatment the patient is free of grand mal seizures at present but he still suffers of occasional spells of laughter associated with myoclonic jerks (see fig. 3).

This patient represents an instance of epileptic laughter associated with massive myoclonic spasm, grand mal seizures, mental retardation and precocious puberty, probably secondary to prematurity and anoxia during the perinatal period.

**Case No. 2** D. F. is a 3-1/2 year-old white boy who was first seen at the age of 6-1/2 months. The child was born after a normal full-term pregnancy and delivery. He remained in an apparent good state of health until the age of 3 months when he developed



Figure 3.—This picture shows patient # 1 during an attack of epileptic laughter.

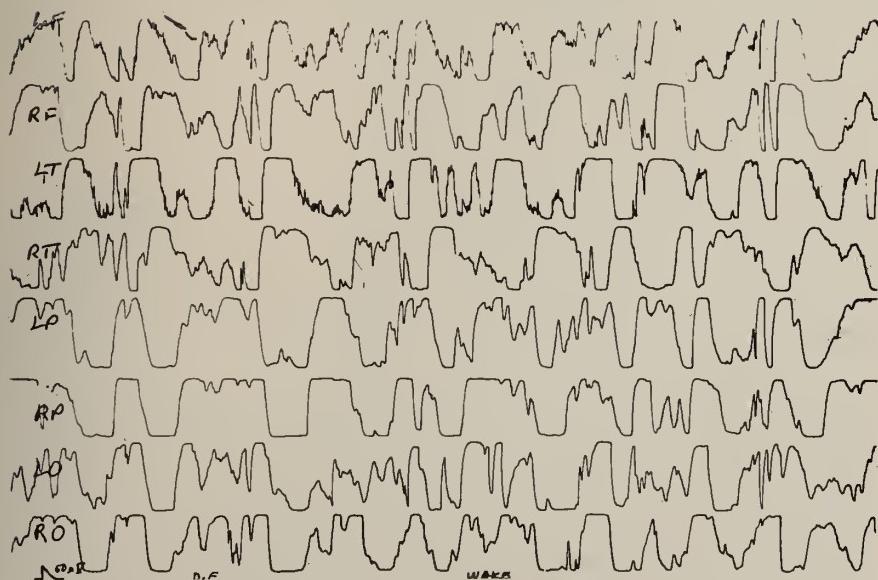


Figure 4.—This is a portion of an electroencephalogram of patient # 2, at age of 6-1/2 months. The pattern is compatible with the electroencephalographic diagnosis of hypsarrhythmia.

an upper respiratory infection that lasted for a week, at the end of which he went into a state of stupor and became seriously ill. He was seen by a pediatrician who diagnosed the illness as encephalitis; however, there was no laboratory confirmation of this diagnosis. While he was recovering from the acute illness he developed massive infantile spasms.

The patient has continued having daily frequent infantile spasms and at the age of 6-1/2 months the child appeared depressed and was unable to support his head. At that time, an electroencephalogram was performed (see fig. 4) which showed findings compatible with hypsarrythmia. At the age of 2 the child developed paroxysmal episodes of compulsive laughter associated with the spells of massive spasm and continued having such seizures every week until the age of 3. The past medical and family histories are non contributory.

Since the age of 6-1/2 months and until 1-1/2 years he was treated with full therapeutic doses of ACTH and corticosteroids. At present there is a definite reduction in the frequency of seizures. He is free of the paroxysmal laughter and only occasionally develops a fit consisting of slight myoclonic spasms or akinetic seizures. He is able to ambulate with some difficulty and seems more aware of the environment than formerly but still appears markedly retarded. (see fig. 5).



Figure. 5—This is a portion of an electroencephalogram performed on patient # 2 at the age of 3-1/2 years. Please note the epileptiform discharges consisting of multiple spikes and slow waves similar to those seen in patient # 1 (see fig. 1).

This second case represents an instance of infantile (myoclonic) massive spasms with epileptic laughter and electroencephalographic diagnosis of hypsarrythmia secondary to an encephalopathy which could have been due to a viral encephalitis at the age of 3 months.

**Case No. 3** This patient is a 33 year old white male who has a history of epileptic seizures since the age of 15. The attacks are preceded by a profound sensation of laughter that he calls "mal de risa". This emotional state, which is similar to the laughter emotion normally experienced in response to a funny situation, is at times associated with an inappropriate smile but no audible laughing and is followed by masticatory and chewing movements during which period the patient is unconscious. Some of these episodes are followed by grand mal seizures that have been witnessed by several people. The patient has noticed that an intense emotional experience is frequently followed several hours later by one of these seizures.

The family and past medical histories are non contributory. The physical and neurological examinations are negative.

We are impressed by the possibility that this case may be one of psychomotor epilepsy due to the presence of the emotion of laughter, the masticatory and swallowing movements and the association with grand mal seizures. However, at this writing we still lack electroencephalographic confirmation. This patient has shown a definite response to diphenylhydantoin and is practically under complete control. This third case most probably represents a patient with psychomotor epilepsy associated with a laughter disorder.

#### DISCUSSION

The three cases reported are instances of epileptic laughter. The first two are associated with massive myoclonic spasms and manifest violent laughing, while the third case shows mere grinning or smiling. The first two patients experience no emotion associated with the laughter but the third patient feels the emotion of laughter but is not conscious of any funny or laughing situation.

The first case of epileptic laughter was reported by Fere<sup>5</sup> in 1898 and this has been followed by a series of scattered reports,<sup>7-15</sup> until the work of Druckman and Chao<sup>16</sup> in 1957, who after reviewing the literature, reported a group of eleven cases. This is the largest series of cases ever reported. This paper is an excellent review of the literature, presents a discussion of the variable clinical and electroencephalographic picture, and a review of the existing functional and pathological evidence. The authors conclude that

there is a definite probability that epileptic laughter is due to an organic cause and they theorize about the possible role of the hypothalamus.

Lennox<sup>14</sup> reported two cases of epileptic laughter that he referred to as compulsive laughter. One was that of a 21 year old student nurse manifesting automatic epilepsy and syncope and showing spikes from the left cerebral hemisphere. The other was that of a medical student manifesting dreamy states and automatism and showing diphasic spikes in the anterior temporal leads in the E.E.G.

The physiological and pathological evidence up to the present is very suggestive of the possibility of a center of laughter localized in the hypothalamus. This center could be irritated by neoplasms growing in this areas as seen in the cases reported by List<sup>2</sup> and LeGross<sup>12</sup> or by the lesion responsible for the massive spasm as seen in the cases of Druckman and Chao<sup>16</sup> and in two of the cases in the present report. Irritation of the center may occur in diencephalic seizures as in the cases of Gibbs<sup>11</sup> and Druckman and Chao,<sup>16</sup> or in psychomotor or temporal lobe seizures as in the cases of Lennox,<sup>17</sup> Druckman and Chao<sup>16</sup> and in our third case.

There is enough clinical evidence accumulated to suggest that an active participation of the centrencephalic regions and of the hypothalamus occurs with the seizures of massive spasm and that the temporal lobe participates in centrencephalic seizures. This evidence points to a widespread coparticipation of the above areas in temporal lobe, diencephalic, centrencephalic and brain-stem seizures. The clinical manifestations and the electroencephalographic pattern in one group of seizures are probably the result, not only of the site of the primary epileptogenic focus, but also due to the presence of secondary foci or the spread of the discharges to related system of neurons.

If the above hypothesis is correct, then the manifestations of a "seizure" are due to the dominance of the area with the largest epileptiform activity and masking of the other regions but not an expression of epileptic activity in one region alone without the participation of the others.

The cases of massive spasms associated with epileptic laughter and precocious puberty suggest that the involvement of the brain stem, responsible for the massive spasm, electrically influences the hypothalamus, or otherwise, there may be hypothalamic lesions associated with the brain-stem damage.

The association of precocious puberty with centrencephalic epilepsy<sup>2,17,19</sup> and with temporal lobe seizures<sup>20,22</sup> is already documented in the literature. The exact mechanism for the above association of symptoms, is not known. We are tempted to theorize

that the temporal lobe and/or the centrencephalic abnormal influences over the hypothalamic area are responsible for the appearance of the precocious puberty.

Recent experimental evidence<sup>23</sup> obtained in both animal and human electrophysiologic observations demonstrates that the hippocampo-amygda structure (part of the rhinencephalon) plays a definite role in the precipitation and maintenance of epileptic attacks, particularly those of the temporal lobe, but also in the centrencephalic seizures. The rhinencephalic system, therefore, is apparently concerned with the alterations of the so-called centrencephalic epilepsy, which in turn, as shown above, might be associated with precocious puberty and/or epileptic laughter.

#### SUMMARY

Forced laughter occurring in a patient without an external precipitant is discussed. The importance of epilepsy as a causative factor is stressed. The authors report 3 cases of epileptic laughter; the first one associated with massive myoclonic spasms, grand mal seizures, mental retardation and precocious puberty; a second case of infantile myoclonic massive spasms with epileptic laughter and a third case of a patient with psychomotor epilepsy associated with a laughter disorder.

A brief discussion involving the history, physiology, pathology and possible localization of this manifestation is presented. The possibility of involvement of the rhinencephalic system is also raised.

#### RESUMEN

Episodios de risa inmotivada sin participación aparente de factores precipitantes situacionales en el medio externo son comentados con especial énfasis para con episodios de risa que aparecen en pacientes que reconocen como factor causal trastornos de naturaleza epiléptica. Los autores informan sobre 3 casos de epilepsia hilarante; un primer caso con espasmos masivos mioclónicos, gran mal, deficiencia mental y pubertad precoz; un segundo caso de mioclonia infantil y un tercero de posible epilepsia sicomotora asociada a desórdenes de risa inmotivada.

Se discute brevemente la historia, fisiología, patología y posible localización de dicho fenómeno. Se plantea asimismo la posibilidad de participación de estructuras rinencefálicas.

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# THE ANTIGENICITY OF INSULIN\*

## A REVIEW

ELENA VILLAVICENCIO SUAREZ, M.D.

### INTRODUCTION

Soon after the discovery of insulin by Banting and Best in November 1921, questions were raised as to its antigenicity. Barral and Roux<sup>1</sup> in 1931 demonstrated the occurrence of anaphylactic reactions in guinea pigs sensitized to beef insulin. Lewis<sup>2</sup> demonstrated the Schultz-Dale reaction in the uteri of sensitized guinea pigs. Uteri sensitized with purified beef insulin reacted when exposed to this substance but did not react in the presence of beef pancreas protein or beef serum. This suggested to them that the insulin protein was distinct from the bulk of the pancreatic protein. Complement-fixation with insulin as antigen was reported by Richardson<sup>3</sup> in 1938, and by Wasserman, Broh-Kahn and Mirsky<sup>4</sup> in 1940. Wasserman et al noticed that although they could develop complement-fixing antibodies in rabbits, these did not develop signs or symptoms of diabetes, so they concluded that these antibodies did not act as antihormone.

For some time interest was centered around the immunologic identity of insulin from various species. This problem was made quite difficult by the fact that at the time the primary structure of the insulin molecule had not been established. Wasserman et al<sup>5</sup> believed that indeed the insulin derived from various animal sources was immunologically identical. Later on Arquilla and Stavitsky<sup>6</sup> pointed out that although there is a great deal of cross reaction between, for example, rabbit antisera to crystalline beef insulin and sheep, beef, and pork insulin, this did not mean that the insulin from various species was identical. This was proved to be true by Harris, Sanger and Naughton.<sup>7</sup> Arquilla made the interesting observation that whether the anti-insulin antisera would react with the different endogenous insulins from the various species tested was difficult to predict. He thought that endogenous insulin could be species specific and in the course of purification and extraction this species specificity could be lost.

For some time insulin was regarded as a weakly antigenic protein, but evidence to the contrary started to accumulate. Banting<sup>8</sup> et al reported the detection of anti-insulin activity as determined by the mouse convulsion assay in a psychiatric patient

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treated with insulin shock. They localized the anti-insulin factor to the serum globulins.

Tuft<sup>9</sup> was probably the first to study insulin allergy carefully. The first insulin preparations had caused a considerable amount of allergic reactions which were due, in part, to the presence of impurities. However, even after better preparations were obtained, allergic reactions continued to be reported. In his work Tuft reported the presence of skin sensitizing antibodies and of a precipitin in a patient's serum. The patient showed allergy to the insulin but not to protein extracts of the animal from which the insulin was derived.

Now interest was centered around the different types of insulin antibodies and their characterization. In 1942 Lowell<sup>10</sup> reported a patient who showed both a skin sensitizing and a neutralizing antibody to insulin. Patients exhibiting both insulin allergy and insulin resistance were found.<sup>11,16,18</sup> It was pointed out that insulin resistance could very well occur on an immunological basis and that it could be associated with the presence in the serum of a neutralizing antibody for crystalline insulin. It was established that the skin-sensitizing antibodies and the insulin neutralizing ones were distinctly different.<sup>12</sup> Interesting cases showing variations in resistance and allergy were described.<sup>13</sup> The serum of a patient having both insulin allergy and resistance was shown to be capable of protecting mice against the hypoglycemic effect of insulin and of passively sensitizing the skin of a normal subject. After heating the serum at 57°C for two hours, the reagin was no longer present although the insulin-neutralizing effects persisted.

The initial idea of insulin being such a poor antigen started to change. Moloney and Coval<sup>14</sup> demonstrated that guinea pigs regularly produced insulin-neutralizing antibodies in response to immunization with crystalline beef or pork insulin and that these antibodies were capable of inducing diabetes by passive transfer to mice. The production of acute insulin deficiency by administration of insulin-anti-serum has been reported by other workers.<sup>15,17,19</sup>

#### INSULIN ALLERGY

As pointed out before, insulin allergy and insulin resistance may co-exist but they are more frequently observed independently. Because sensitivity to contaminating substance is much more frequent than the insulin allergy, it is important to establish a diagnosis. Use of repeatedly re-crystallized insulin may help in this respect.

Insulin allergy is characterized by urticaria, itching, angio-

neurotic edema or even anaphylactic shock. The patient will show a positive scratch test and his serum will frequently contain antibodies capable of sensitizing normal skin by passive transfer. The skin-sensitizing antibody persists over a period of six months.<sup>13</sup>

Loveless and Cann<sup>20</sup> isolated the skin-sensitizing antibody in the betaglobulin. The passive transfer of insulin sensitivity to the skin of a normal subject by intradermal injection of the reagent could be blocked by addition of the heat-inactivated serum to the insulin prior to injection. Thus, the "blocking" antibody was heat stable. It was assumed that the "blocking" antibody and insulin-neutralizing antibody were identical, but this question remains unsettled because of reported differences in electrophoretic migration.

Allergy to human insulin has been demonstrated. The skin-sensitizing antibody is heat labile.<sup>10</sup>

#### INSULIN BINDING ANTIBODIES

In 1956, Berson and Yalow reported that insulin-I<sup>131</sup> was degraded in vivo much more slowly in patients treated with insulin than in diabetics who were not taking insulin.<sup>21</sup>

Insulin-binding antibodies are present in the serum of almost all humans treated with insulin for six weeks or longer. It was demonstrated by means of paper and starch block electrophoresis, by paper chromatography and by ultracentrifugal analysis of plasma-I<sup>131</sup> that the labeled insulin is bound to insulin-binding antibody in the plasma of treated subjects.<sup>22</sup> Due to this the insulin is restricted from easy passage, whereas in non-treated persons the small unbound insulin molecule is permitted readily to escape from the blood stream and be rapidly metabolized.

The presence of insulin-binding antibodies was confirmed by Skom and Talmage who showed that rabbit anti-human serum globulin precipitated I<sup>131</sup> labeled insulin in the sera of treated subjects.

Berson and Yalow have been able to demonstrate insulin antibodies by means of paper electrophoresis. Under these conditions free insulin, in common with many other proteins, possesses the capacity to adsorb on certain inert material such as paper and, when applied in low concentration to paper strips for electrophoresis or chromatography, remains at the site of application ("origin"). This adsorption is readily detected when the serum proteins are caused to migrate away from the origin.

In insulin-treated cases, the labeled insulin is found to migrate in whole or in part with serum proteins just in advance of the beta-globulins.

On starch block electrophoresis insulin migrates with a mobility almost as great as that of serum albumin in normal patients, but in the sera of insulin-treated patients the insulin is bound to the globulins.

Since insulin is a smaller molecule than albumin, it sediments less rapidly in normal serum, but it sediments with the globulins in the sera of insulin-treated subjects.

In the majority of diabetic subjects treated with insulin, the concentration circulating insulin-binding antibody is such that the insulin-binding capacity of the plasma is usually less than 10 units per L. plasma. The insulin-binding capacity of plasma in severe chronic insulin resistance is almost always greater than 60 units per L. plasma.

In order to be able to relate insulin requirements to antibody concentration, we have to inquire about the fate of antibody-bound insulin. It is important to consider the rate of disposal of insulin-antibody complexes. In precipitating antigen-antibody systems, these large aggregates are removed very rapidly. However, insulin-antibody complexes have been found to be non-precipitating,<sup>24</sup> though positive precipitin reactions have been obtained.<sup>25,26</sup> Because of this their intra-vascular life span is considerably longer than that of precipitating systems.

Based on previous work done by Weigle<sup>27</sup> in animals, Yalow and Berson<sup>28</sup> have estimated that in non-resistant subjects, even if all antibody present remained continually saturated with insulin, the additional insulin required to compensate for immunologic wastage would be small. However, in resistant subjects this could account for insulin requirements of many hundreds of units daily.

We must also consider that not all antibody-bound insulin is destined for immunologic elimination since insulin-antibody complex formation is reversible by dissociation<sup>22</sup> and the rate of release of insulin varies. Berson and Yalow have done a most elegant study of the kinetic aspects of this problem.<sup>29</sup> A certain fraction of the dissociated insulin will rebind to antibody if there is a significant excess of uncomplexed antibody molecule; some will go to the extravascular sites. Here again a fraction will be bound, but some will exert its hormonal effects or will be degraded.<sup>30</sup> Antibody-bound insulin has been shown to be inhibited by insulinase.<sup>31</sup> The dissociation of bound insulin appears to be responsible for late hypoglycemic reactions occurring after therapy with massive doses of insulin. Periodic obligatory abandonment of insulin therapy due to high percentage of insulin-binding antibody has also been reported.<sup>32</sup>

Thus, to interpret insulin requirements in insulin resistance we must take into consideration (1) antibody concentration,

(2) rate of elimination of insulin-antibody complexes and, (3) kinetic factors involved in complex formation. There is no strict correlation between antibody concentration and insulin dosage, though in general patients taking more insulin exhibit highest antibody titers.

#### INSULIN IMMUNOASSAY

At the University of Minnesota an insulin assay has been developed for the determination of plasma insulin levels.<sup>39</sup> Taking advantage of the fact that human insulin cross reacts with insulin-binding antibodies in guinea pigs immunized with crystalline beef insulin, anti-insulin anti-bodies are produced in these animals. Insulin will form a soluble complex with this antibody. In the second step, this soluble complex is precipitated by antibody to guinea pig serum, which is obtained from rabbits. Insulin-I<sup>131</sup> in tracer doses is used. It will compete with the unknown serum insulin for the antibody. As increasing amounts of unlabeled insulin are added, the percent of I<sup>131</sup> insulin in the precipitate is decreased correspondingly.

Insulin antibodies have also been used to demonstrate insulin in the islets by the Coons technique.

There are still too many shadows surrounding the problem of insulin antibodies. I do not think these play a part in the etiology of Diabetes, as they have not been demonstrated in patients who have not had any insulin therapy. They seem to play a role in insulin-resistance. They may also help to explain the increased insulin requirements in patients developing an infection. Extreme insulin sensitivity may be due to low levels of insulin-binding antibodies. Before we can define clearly the relationship between insulin-binding antibodies and the clinical management of diabetic patients, further study of these problems are needed.

#### SUMMARY

The subject of antigenicity of Insulin has been reviewed in light of the present clinical and experimental data. The presence of antibodies to insulin has been detected by direct skin sensitization,<sup>9</sup> passive cutaneous sensitization,<sup>9</sup> the Schultz-Dale reaction,<sup>2</sup> complement-fixation,<sup>33</sup> precipitation,<sup>25,26</sup> hemagglutination,<sup>34</sup> anaphylactic reaction,<sup>1</sup> in vivo insulin neutralization,<sup>10</sup> insulin-binding<sup>23</sup> and by the blocking reaction.<sup>20</sup>

Of these, the atopic reagent is responsible for the direct and indirect skin-sensitivity. The inter-relationships of the remaining antibody reactions is uncertain. Berson and Yalow<sup>29</sup> came to the

conclusion that apparently insulin is univalent in its reaction with antibody and that there are at least two orders of antibody—combining sites. They state that univalence of insulin is not necessarily equated with monoantigenicity. Whether insulin-neutralizing, insulin-binding and insulin blocking antibodies are equal seems likely, but remains to be proven. The skin-sensitizing antibody is heat-labile and can be obtained from the beta-globulin fraction of serum from affected individuals. The insulin-binding antibody is heat-stable and can be demonstrated in the gamma or inter gamma-beta globulin in patients previously treated with insulin.

#### RESUMEN

Se ha observado en pacientes la ocurrencia de alergia y de resistencia a insulina. Se ha demostrado que aunque ambas condiciones pueden coexistir, cada una es producida por un anticuerpo diferente. La resistencia a insulina es producida por un anticuerpo no-precipitante. Esto hace que estos complejos tengan una vida intravascular prolongada. La concentración del anticuerpo y la rapidez con que se eliminan los complejos insulina-anticuerpo afectarán los requerimientos de insulina en un paciente diabético. Este anticuerpo aparentemente no juega papel etiológico en la diabetes, ya que no se ha demostrado en pacientes diabéticos que no han recibido insulina.

La alergia a insulina es producida por otro anticuerpo. Este último es destruido por el calor y se puede obtener en las betaglobulinas.

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**HYPERTENSION DUE TO UNILATERAL RENAL  
VASCULAR DISEASE**

In the last few years it has been recognized that there are multiple causes of correctable hypertension. Among these are included pheochromocytoma, primary aldosteronism, Cushing's syndrome, coarctation of the aorta and unilateral vascular renal disease. Recent statistics show that unilateral renal disease may be responsible from 2 to 25% of all cases of sustained hypertension.<sup>1</sup> Dustan and Page reported in 1962 that out of 617 hypertensive patients, 173(28%) had renal vascular occlusive disease.<sup>2</sup> In view of this, the physician should be on the look out for this illness as with the recent surgical measures there is much to be offered to some of these patients.

The presence of hypertension in a young patient who has not had glomerulonephritis, the sudden onset of hypertension especially if accompanied by abdominal or flank pain with or without a history of recent trauma, the development of unexplained polyuria with concurrent albuminuria, the presence of an audible abdominal bruit or the presence of hypertension of sudden onset in an elderly patient, should make you suspicious of the possibility of unilateral vascular renal disease. The presence of long duration of the hypertension should not incline the physician to eliminate an investigation of the kidneys as a cause.

The presence of sudden flank pain with the onset of hypertension, pyrexia, leucocytosis, vomiting, albuminuria and hematuria is suggestive of renal embolization with sudden segmental or total renal ischemia or infarction.

Hypertension due to unilateral renal vascular disease might be caused by renal artery stenosis, fibromuscular hyperplasia, arteriovenous fistula, multiple renal arteries, arteritis, renal artery aneurysm, renal infarction and atherosclerotic occlusion of renal arteries.

Certain laboratory tests are useful in establishing the diagnosis. A flat plate of the abdomen may reveal a decrease in size in one of the renal silhouettes which will require further investigation. Intravenous pyelogram might be normal or abnormal. Whenever there is a total occlusion of a single main renal artery no visualization of the dye on the affected kidney shall be expected. In some instances of ischemia in one kidney early rapid films might reveal a delay in the visualization of the affected kidney by the contrast medium. In the presence of a non visualized

kidney, a normal retrograde pyelogram will suggest the presence of unilateral renal vascular disease.

Divided or so called split renal function studies are most helpful in establishing the diagnosis. These are based upon cystoscopy and catheterization of each individual kidney for the study of the amount of flow in urine in each kidney per unit of time and for the analysis of samples obtained from each kidney for different substances among which are sodium, inulin, para-amino hippurate, hippuran, PSP, creatinine, etc.<sup>3,9</sup> In cases of multiple renal vessels originating from the aorta to supply one kidney or in cases of early renal hypertension these studies might be normal. Split function studies are specially useful in renal artery stenosis. Whenever there is bilateral renal arterial disease these tests are not very useful.

The method of renographic studies with the use of minute amounts of  $I^{131}$  tagged contrast media injected intravenously depends upon its accumulation and excretion by the kidneys so that the radioactivity emanating from each kidney can be measured. Three different types of abnormal renograms can be obtained in unilateral renal hypertension: an abnormal vascular spike, a prolonged evaluation phase and obstruction.

A renal scintigram may be used. In this procedure Neohydrin tagged with mercury-203 or 197 is injected intravenously. This radioactive substance will remain in the kidney parenchyma for a period of time permitting a mapping of the kidneys with a photoscanner. A defect in the kidney map obtained (cold spot) is suggestive of renal infarction or tumor.

One of the most useful procedures is renal arteriography. This procedure is usually performed by the translumbar puncture of the abdominal aorta or by retrograde catheterization of the abdominal aorta through the femoral route.<sup>10</sup> This test is performed with the use of a radiopaque dye injected under pressure and requires the recording of the x-ray films with a serigraph. This is the only method that permits visualization of the renal vascular tree and the demonstration of the lesions when present.

Some instances of unilateral renal disease are accompanied by a picture of hyperaldosteronism manifested by polyuria, alkalosis and a marked loss of potassium in the urine with the development of hypokalemia with its clinical manifestations.

Different theories have been postulated to explain the development of hypertension in unilateral vascular renal disease. There seems to be agreement upon the fact that alterations in the juxtaglomerular cells in the wall of the afferent arterioles of the kidneys in some way lead to production of renin.<sup>11</sup> Renin eventually leads to the formation of angiotensin and hypertension.<sup>12</sup> Whether

the initial precipitating mechanism is a decrease in renal blood flow to the affected kidney or alterations in the intrarenal arterial pulse pressure and the pulsatile flow without changes in the renal blood flow has not been clarified.<sup>13</sup>

Today, there are many surgical corrective procedures that can be offered to some of these patients. These include resection of atheromatous plaques, bypass of occluded or stenosed arteries, removal of arterial aneurysm, partial resection of ischemic or infarcted areas of the kidney or even nephrectomy.<sup>14-15</sup> Effective medical management with hypotensive drugs can be obtained in some patients but medical treatment should not be a substitute for indicated reconstructive renovascular surgery in patients without medical contraindications to the operative procedure. The practicing physician should be aware of unilateral vascular disease leading to hypertension in order to insure that any possible suspect receives the benefit of an adequate and reliable work up in order to decide if his hypertension can be corrected.

Mario R. García Palmieri, M.D.

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## PRINCIPLES OF MEDICAL ETHICS

### SECTION 1

The principal objective of the medical profession is to render service to humanity with full respect for the dignity of man. Physicians should merit the confidence of patients entrusted to their care, rendering to each a full measure of service and devotion.

#### 1. Character of the physician

The prime object of medical profession is to render service to humanity; reward or financial gain is a subordinate consideration. Whoever chooses this profession assumes the obligation to conduct himself in accord with its ideals. A physician should be "an upright man, instructed in the art of healing." He must keep himself pure in character and be diligent and conscientious in caring for the sick. As was said by Hippocrates, "He should also be modest, sober, patient, prompt to do his whole duty without anxiety; pious without going so far as superstition, conducting himself with propriety in his profession and in all the actions of his life." (*Principles of Medical Ethics, 1955 edition, Chapter I, Section 1.*)

#### 2. Ability of patient to pay

One of the strongest holds of the profession on public approbation and support has been the age-old professional ideal of medical service to all, whether able to pay or not. That ideal is basic in our ethics. The abandonment of that ideal and the adoption of a principle of service only when paid for would be the greatest step toward socialized medicine which the medical profession could take. All our arguments as to better service to the people, freedom of choice of doctors would be as naught if such service were not available to a vast proportion of the people. (*House of Delegates, 1934*)

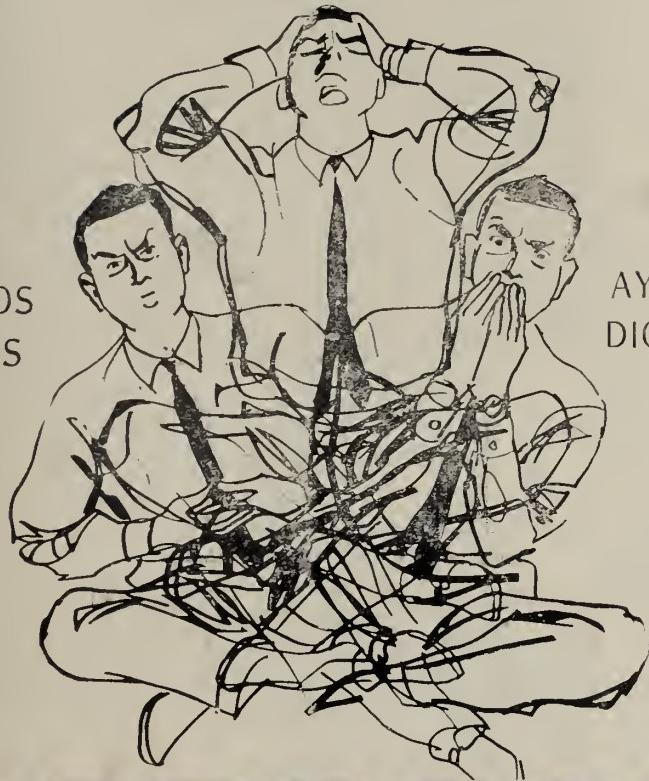
#### 3. Free choice of physician

Free choice of physician is defined as that degree of freedom in choosing a physician which can be exercised under usual conditions of employment between patients and physicians. The interjection of a third party who has a valid interest, or who intervenes between the physician and the patient does not *per se* cause a contract to be unethical. A third party has a valid interest when, by law or volition, the third party assumes legal responsibility and provides for the cost of medical care and indemnity for occupational disability. (*Principles of Medical Ethics, 1955 edition, Chapter VII, Section 4.*)

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## THE PROPERTIES OF OLIVE OIL

by Dr. F. María Segovia de Arana

"Thus, olive oil is unique among vegetable oils by reason of its organoleptic characteristics. Its natural aroma and taste are regarded pleasant by the consuming public in all countries. It need not be refined: it is the only oil that can be consumed in the West in its natural state. This is most important, because in the course of refinement, oils are to some extent transformed and lose some of their nutritive properties."

### COMPOSITION AND CHEMICAL PROPERTIES OF OLIVE OIL

"In the chart below, taken from Hilditch (The chemical constitution of natural fats) the composition in saturated fatty acids (miristic, palmitic and stearic and non saturated (oleic and linoleic) of olive oil in various countries is shown.

#### OILS.

	Miristic	Palmitic	Stearic	Oleic	Linoleic
Italy (Tuscany)	1,1	9,7	1,0	79,8	7,5
Córcica	1,1	9,4	2,0	84,5	4,0
California	1,1	7,0	2,3	85,8	4,7
Spain	0,2	9,7	1,4	81,6	7,0
Tunis	1,1	14,7	2,4	70,3	12,2
Palestine	0,5	10,0	3,3	77,5	8,9
Greece (Rhodes)	0,4	19,7	0,3	69,6	10,4

As can be seen, olive oil, apart from containing a large proportion of a non saturated fatty acid, of twofold linkage, namely oleic acid, also contains lesser quantities of others that have more than a twofold linkage."

## PHITOSTERINES

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## ARTERIOSCLEROSIS AND OLIVE OIL

"The experiments carried out by Dr. Bronte Stewart in South Africa, demonstrated that cholesterol in the blood increased when the subjects consumed animal fats, but this did not occur with vegetable fats, such as sunflower oil, olive oil, etc.

The same type of result was achieved by a group of investigators (among others, Dr. P. D. White, President Eisenhower's personal physician, and Dr. Keys) in a test carried out in Calabria and Crete on subjects whose ages varied between 45 and 65 years and the fatty part of whose food consisted almost entirely of oil. Only two out of the 657 persons examined were seen to have had heart attacks. When this group was compared with a similar one, as regards age, in the United States, whose diet largely included large quantities of animal fats, sixty cases of heart attacks were discovered.

("Time" magazine, 30 December 1957)."

## CONCLUSIONS OF THE WORK OF DR. SEGOVIA DE ARANA

"We must be careful and only recommend such things as can reasonably be expected to do more good than harm. In our opinion, the following measures are reasonable and well founded:

- 1) Reduce the total consumption of calories and in particular those derived from fats, to the amounts consumed, (and which quantities should be maintained) when the body weight is normal between twenty one and twenty five years of age. It is advisable to use non saturated vegetable oils in lieu of animal fats.
- 2) Take active daily physical exercise.
- 3) Avoid all excess (tobacco, alcohol, emotional tension) but such habits need not be cut down drastically.
- 4) Treat arterial hypertension if it appears."

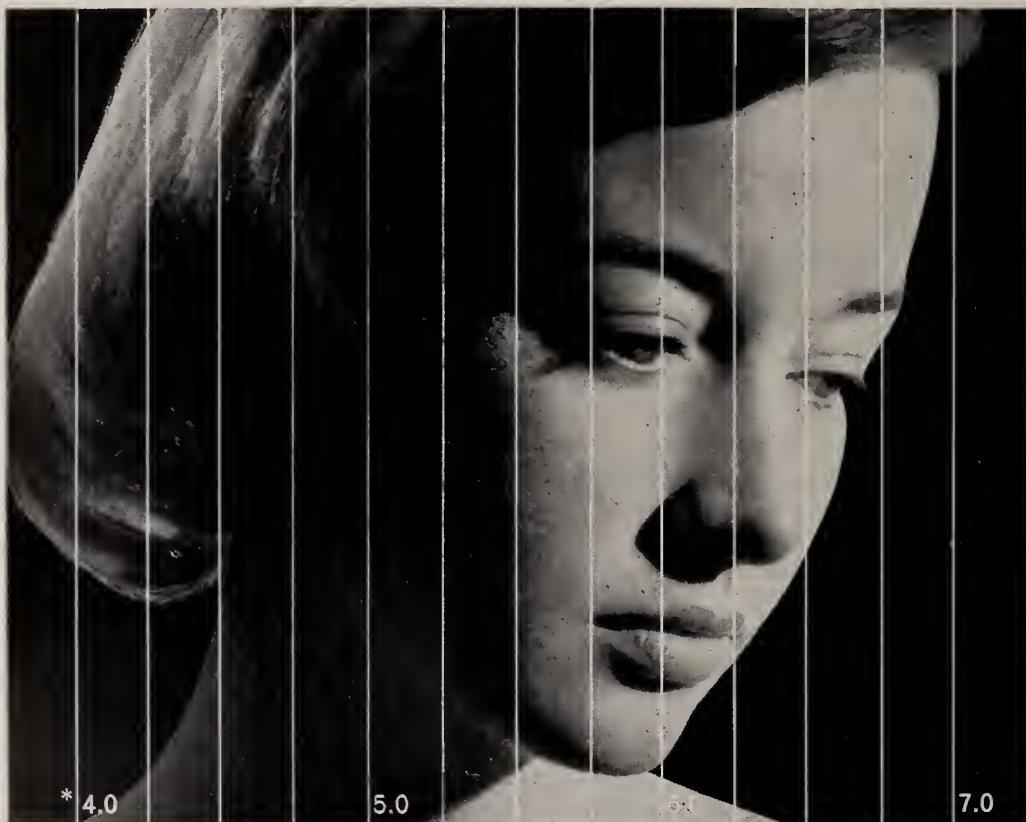
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of hypersensitivity may be observed occasionally. In extremely rare instances, anaphylaxis has occurred following the use of erythromycin.

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Fundado en el 1903 y publicado mensualmente en San Juan, Puerto Rico

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c) Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: (1) introducción, (2) material y métodos, (3) resultados, (4) discusión, (5) resumen (en español e inglés), (6) referencias.

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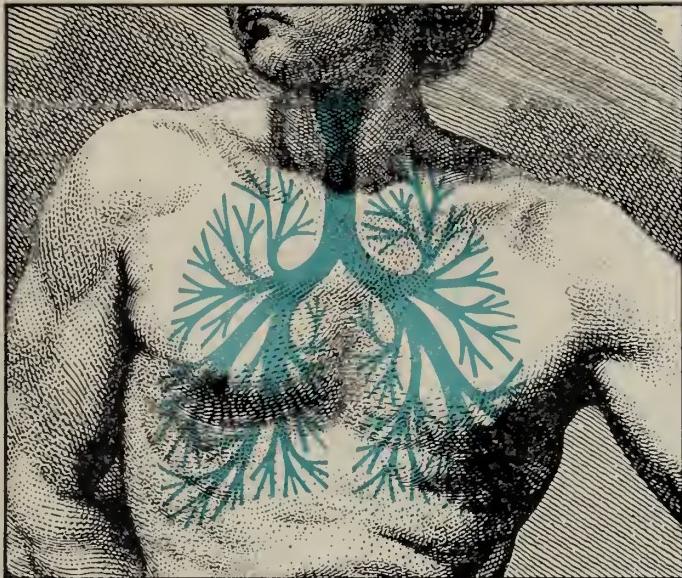
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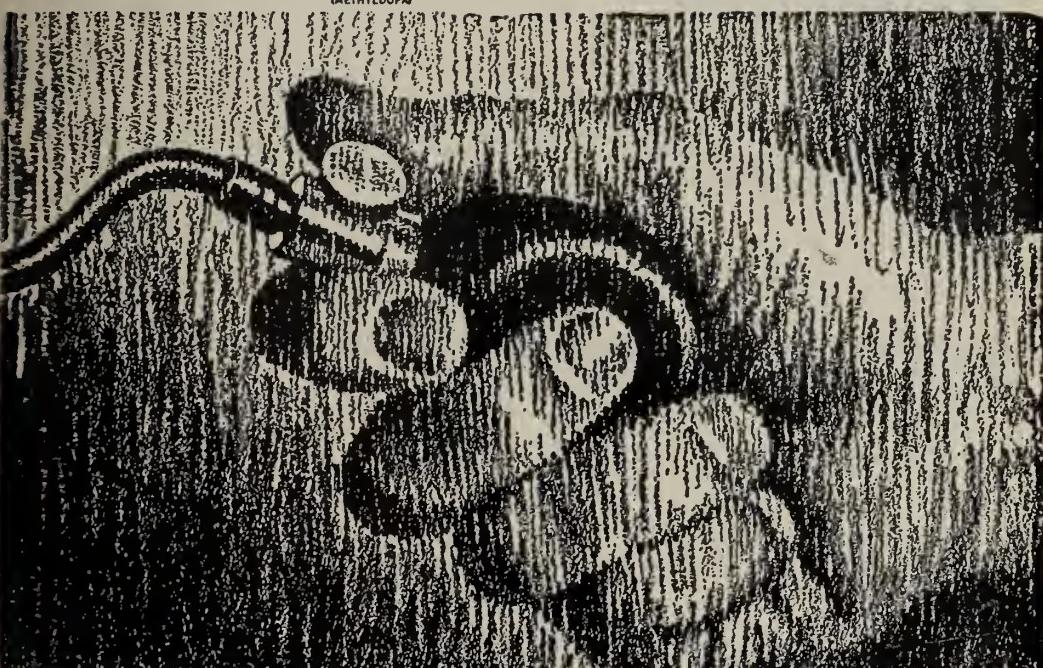
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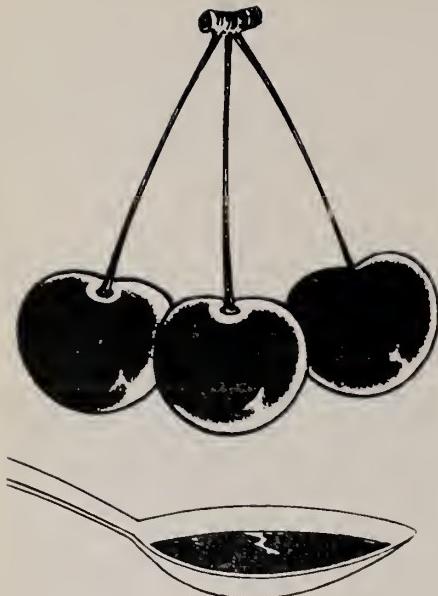
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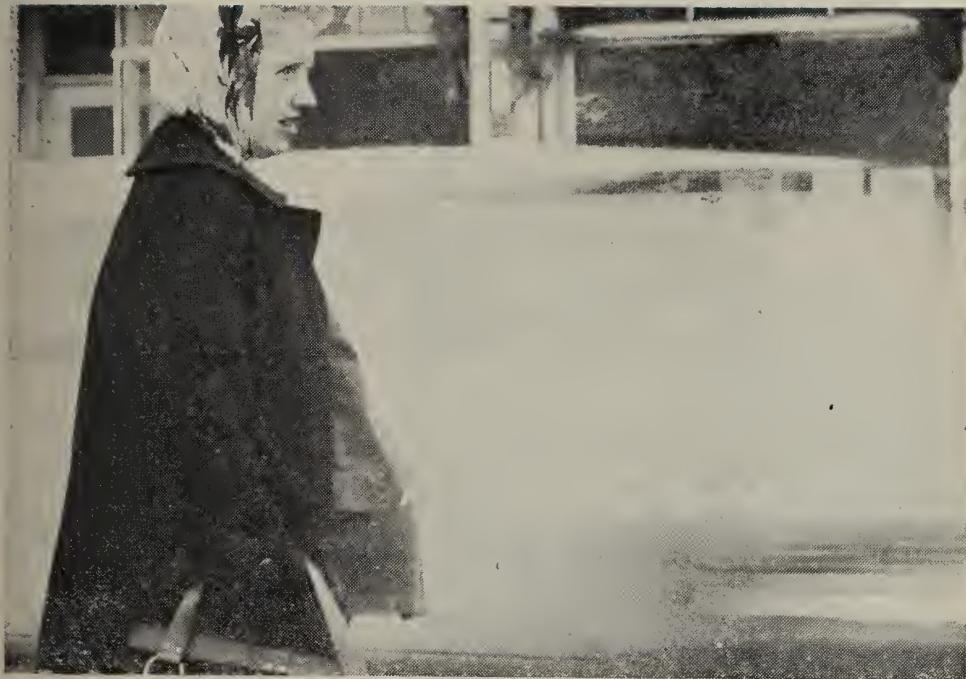
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### Lieberman, A., and Guglielmelli, S.: Persantin®—A Double Blind Study. *Angiology* 15:290, 1964.

Method: A total of 128 hospitalized patients, the majority in severe congestive failure, were studied. Most were 40 to 60 years old. Fifty-nine received dipyridamole, 25 mg. q.i.d., and 69 received placebo tablets q.i.d., for 2 to 3 months in most cases. Routine therapy was continued as needed in both groups.

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### Neumann, M., and Luisada, A. A.: Effect of Rapid- and Slow-Acting "Coronary" Drugs on Precordial Pain of the Aged. *Am. J. M. Sc.* 247:156, 1964.

Method: In a double-blind study, 33 elderly patients with chronic angina pectoris received placebo, dipyridamole 50 mg. t.i.d., and other coronary drugs, each for a 6-week period. The number of nitroglycerin tablets consumed in the last 2-week period was compared for each test preparation.

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2. Wirecki, M.: Dipyridamole: Evaluation of Long-Term Therapy in Angina Pectoris. *Current Therap. Res.* 5:472, 1963.
3. Gaddy, C. G.: Long-Term Treatment of Myocardial Ischemia. *Virginia M. Month.* 91:155, 1964.
4. Griep, A. H.: Nocturnal Angina Pectoris. *GP* 29:78, 1964.
5. Wheatley, D.: Prophylactic Drug Therapy of Angina Pectoris in General Practice. *Proc. Fourth World Congress of Cardiology* IVB:130, 1962.

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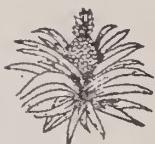
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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



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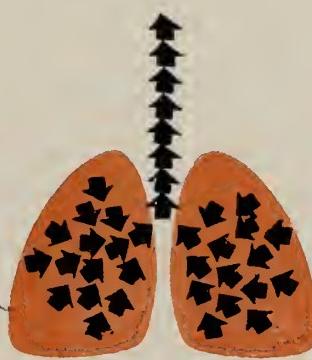
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**Dosage:** While 1 HYDROMOX quinethazone tablet (50 mg.) daily usually suffices, it may be necessary to raise

dosage up to 4 tablets daily (usually spaced) to elicit satisfactory response. When given with other antihypertensives, lower dosages of both agents may suffice.

**Side Effects:** Skin rash, GI disturbances, weakness or dizziness may occur, usually controllable by reducing dosage or correcting electrolyte imbalance. Pre-existing electrolyte abnormalities may be aggravated. Possibility of potassium depletion is greater in cirrhotics and digitalized patients. Foods rich in potassium may be desirable. Possibility of azotemia is greater in renal disease; and of hyperglycemia and glycosuria in diabetes. Photoallergy and hyperuricemia predisposing to gout have occurred. There may be a sudden drop in blood pressure when given with ganglionic blocking agents, veratrum or hydralazine, requiring reduction in dosage of these other drugs.

**Precautions:** Anuria.

\*From clinical data on file at Lederle Laboratories. Posed by model.

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# BOLETIN

DE LA ASOCIACION MEDICA DE PUERTO RICO

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NOVIEMBRE, 1964

NO. 11

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## HISTOPLASMOSIS EN PUERTO RICO

### Repaso e informe de un brote contraído en las Cuevas de Aguas Buenas.

JOSE E. SIFONTES, M.D.\*

MANUEL E. SOTO VIERA, M.D.\*

GLADYS TORRES DE BLASINI, PhD.\*\*

La histoplasmosis es una micosis sistémica causada por el hongo *Histoplasma capsulatum*.<sup>1</sup> La infección en el hombre ocurre por inhalación de esporas del hongo. Este se encuentra y crece en el suelo que sirve de fuente de infección al ser inhaladas las esporas del hongo suspendidas en el aire. Son portadores del hongo animales tales como roedores, perros, gatos, murciélagos y caballos, pero no hay evidencia de que estos transmitan la enfermedad directamente al hombre o de que pueda haber contagio de la enfermedad por contacto de una persona con otra. Todas las epidemias de histoplasmosis que se han informado han sido por inhalación de polvo contaminado con *Histoplasma capsulatum*.

**Manifestaciones Clínicas** — Despues de inhalar las esporas, el período de incubación puede ser desde cinco días hasta varias semanas. En las tres cuartas partes de los casos es de 8 a 15 días. Se cree, pero no se sabe con certeza, que en las dos terceras partes de los casos la infección primaria es asintomática. La forma más común de la enfermedad es la lesión pulmonar aguda que se ve principalmente en niños. Los síntomas son: fiebre, tos, malestar, escalofríos, dolor de cabeza y dolores torácicos y musculares. A la exploración física los hallazgos son mínimos, pudiendo oírse a veces estertores, sin otras alteraciones de importancia. La radiografía de tórax puede demostrar infiltraciones bilaterales, adenopatías hiliares y raras veces derrames pleurales o segmentos

\* Del Departamento de Pediatría, Escuela de Medicina, Universidad de Puerto Rico.

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atelectáticos. La evolución, casi siempre, es benigna, siendo la duración de los síntomas desde varios días hasta varios meses.

La evolución desfavorable de la histoplasmosis es rara. En niños, el cuadro clínico es el de histoplasmosis diseminada que se caracteriza por fiebre, anemia, hepatosplenomegalia, linfadenopatía generalizada, púrpura y lesiones necróticas o ulceradas. Otra forma de evolución desfavorable es la de lesiones pulmonares crónicas. Estas se ven principalmente en adultos y el cuadro clínico y radiográfico no se puede distinguir del de la tuberculosis pulmonar sin hacer pruebas cutáneas, serología y cultivos.

**Infección, mortalidad y morbilidad en Puerto Rico**— La prevalencia de infección por histoplasmosis se ha estudiado mediante la prueba de histoplasmina. En el 1951 Suárez y colaboradores demostraron una prevalencia de 12.7% de reacciones positivas a la histoplasmina entre 1055 sujetos examinados en Puerto Rico.<sup>2</sup> Hemos realizado encuestas más recientes que han confirmado los hallazgos iniciales de Suárez. Entre niños hospitalizados en el Departamento de Pediatría del Sanatorio A. Ruiz Soler el 4.6% dieron reacciones positivas a la histoplasmina en el 1957. Entre adultos del Sanatorio de Cayey hospitalizados bajo tratamiento por tuberculosis activa el 35.7% dió reacción positiva a la histoplasmina en ese mismo año. En el 1955 en una encuesta de escuelas representativas, seleccionadas en toda la isla de Puerto Rico, la prevalencia de reactores positivos en niños de primer grado cuya edad promedio era de 7-1/2 años variaba desde 0% hasta 70.6% en una escuela rural de Mayagüez. En diferentes escuelas del mismo pueblo variaba grandemente la prevalencia de reactores a la histoplasmina. Por ejemplo en Mayagüez, donde se encontró la escuela con la más alta prevalencia en toda la isla, también se encontró una escuela donde no había un sólo reactor a la histoplasmina. Entre estudiantes de nuestra Escuela de Medicina, en el 1964 el 32.6% tenían reacción positiva a la prueba de histoplasmina.

El grado de infección por histoplasmosis en una población se ha estudiado indirectamente midiendo la prevalencia de calcificaciones visibles en la radiografía del tórax de personas con reacción negativa a la prueba de tuberculina. La presunción es que si estas calcificaciones no son debidas a tuberculosis, lo más probable es que la mayoría sean debidas a histoplasmosis. Hemos estudiado 2,275 radiografías de personas sanas de todas las edades con tuberculina negativa encontrando que el 7.8% tenían calcificaciones. Al analizar estos datos por pueblo se encontró que el porcentaje más alto era en Juncos con 19.6% y el más bajo en Fajardo con 2% (Tabla I).

La mortalidad por histoplasmosis en Puerto Rico no es conocida. En otras partes del mundo, se sabe que no es alta.<sup>3</sup> El úni-

TABLA I

Evidencia Radiográfica de Calcificaciones Pulmonares Entre Personas  
Con Reacción Negativa a la Prueba de Tuberculina

Pueblo	Número de Personas Examinadas	Número con Calcificaciones	Porcentaje con Calcificaciones
Aguadilla	76	4	5.3
Arecibo	294	24	8.2
Bayamón	390	30	7.7
Caguas	214	30	14.0
Cayey	207	7	3.4
Fajardo	50	1	2.0
Humacao	128	7	5.5
Juncos	51	10	19.6
Manatí	216	17	7.9
Río Piedras	317	29	9.1
Santurce	223	12	5.4
Mayagüez	74	4	5.4
Ponce	35	2	5.7
TOTAL	2275	177	7.8

co caso de muerte por histoplasmosis en Puerto Rico fue informado por De Jesús y colaboradores<sup>4</sup> en una niñita de 3 años, de Caguas, que presentaba un cuadro clínico de anemia, edema, ascitis, linfadenitis, hepatoesplenomegalia, hipoproteinemia, trombocitopenia y evolución fatal. En la autopsia se encontró el Histoplasma capsulatum en el bazo, glándulas linfáticas e hígado.

La enfermedad por histoplasmosis en Puerto Rico es probablemente común, aunque es probable que la mayoría de los casos no se estén diagnosticando por ser benigna. En el 1960, Torres de Blasini y colaboradores informaron el primer caso comprobado en un adulto.<sup>5</sup> Se trataba de un varón de Gurabo, de 62 años, con una lesión cavitaria en el lóbulo superior derecho, prueba de histoplasmina positiva, serología positiva para histoplasmosis y cultivo de lavados bronquiales positivos para histoplasmosis.

En el 1961 estudiamos 800 casos diagnosticados como tuberculosis inactiva encontrando 8 con tuberculina negativa y prueba de histoplasmina positiva, lo que nos hacía sospechar que estos pacientes tenían cambios radiográficos por histoplasmosis y no por tuberculosis.

En la clínica de enfermedades pulmonares en niños del Hospital Universitario hemos observado frecuentemente niños con adenopatías hiliares o mediastinales, tuberculina y prueba de Battey negativas e histoplasmina positiva. Son ya numerosos los niños

que estamos observando por histoplasmosis pulmonar aguda benigna procedentes de diferentes sitios de la isla desde Mayagüez hasta Villalba.

**Brote de histoplasmosis en Puerto Rico**— A principios de 1963 tuvimos la oportunidad de ver dos niños de 14 y 15 años respectivamente con un cuadro de tos, fiebre y neumonitis. Uno de ellos presentaba además eritema nudosa. Ambos niños tenían la tuberculina negativa usando el PPD a 5 unidades, la prueba de Battey negativa y la prueba de histoplasmina fuertemente positiva. Pudimos descubrir que ambos niños asistían a la misma escuela privada y que ambos habían visitado las Cuevas de Aguas Buenas en una excursión del Club de Español dos meses atrás. Sospechamos un brote de histoplasmosis entre los excursionistas y decidimos hacer una investigación epidemiológica.

**Materiales y métodos**— Se decidió examinar simultáneamente a todos los excursionistas, y a un grupo de niños testigos de la misma escuela y de los mismos grados, para eliminar la posibilidad de que la fuente de contagio estuviera en la escuela. Después de varias reuniones con las autoridades escolares y los padres de los niños, se obtuvo el permiso necesario para examinar a los excursionistas y a un grupo de niños que no había ido a las Cuevas. También se comprobó que la escuela y las cuevas eran los únicos dos sitios que todos los excursionistas habían visitado.

Exceptuando los dos casos de neumonitis a quienes se les había hecho la prueba de histoplasmina previamente, se obtuvo serología sin prueba de histoplasmina previa en todos los demás excursionistas. Se le hizo histoplasmina (1-100) a todos los niños testigos y excursionistas. A los que dieron reacción positiva a la prueba de histoplasmina se le tomó radiografía de tórax, se le hizo prueba de Battey para Micobacterias anacromogénas, prueba de tuberculina usando el PPD a dosis de 5 unidades y se investigó la sintomatología en el intervalo desde la visita a las Cuevas hasta el examen, cuatro meses más tarde. Los antígenos fueron obtenidos de la oficina de investigaciones del Departamento de Salud Pública Federal.

Luego del estudio epidemiológico entre los excursionistas y testigos, dos de los autores se hicieron prueba de histoplasmina y visitaron las Cuevas con el propósito de explorarlas y obtener muestras para cultivo de *Histoplasma capsulatum*.

**Resultados**— Todos los niños testigos dieron resultados negativos a la prueba de histoplasmina.

Los resultados de los exámenes en los excursionistas aparecen en la Tabla II. De los 14 excursionistas, todos dieron resultados negativos a la prueba de tuberculina y 13 dieron resultados posi-

vos a la prueba de histoplasmina, siendo en todos los casos las reacciones de 10 mm. o más de diámetro. De los 13 con histoplasmina positiva, 9 dieron resultados negativos a la prueba de Battley y 4 resultados débilmente positivos, de 6 a 7 mm. de induración. Este tipo de reacción, según hemos señalado en informes previos, es común en Puerto Rico.<sup>6</sup>

El examen radiográfico excluyendo los dos casos inicialmente observados por neumonitis demostró aumentos en la trama o probables calcificaciones pulmonares en 7 de los niños.

Las pruebas serológicas para histoplasmosis demostraron aumentos de más de 1 en 8 en siete de los niños. El hecho de que los títulos de la prueba de fase de levadura estaban elevados en los dos casos de neumonitis (número 1 y 11) sugería que el aumento no era debido a la prueba intracutánea previa.<sup>7</sup> Los aumentos en los títulos para blastomicosis probablemente representaban reacciones cruzadas con histoplasmosis. La prueba de aglutinación de latex para histoplasmosis demostró aumentos de más de 1 en 8 en dos de los niños.

La evolución de todos estos pacientes al cabo de un año ha sido favorable sin tratamiento específico alguno.

La reacción inicial a la histoplasmina de los dos autores que visitaron las cuevas fue de 0 mm. Se encontró que hay varias cuevas a diferentes niveles y con varias entradas. Tienen bóvedas que llegan hasta 50 pies de altura y están habitadas por innumerables murciélagos. Son sumamente amplias, hasta el punto que están rotuladas como refugios contra radiación por la Defensa Civil. Aunque no fue posible cultivar el hongo, probablemente por la cantidad insuficiente de muestras obtenidas, sí ocurrió en ambos autores un viraje de la prueba de histoplasmina de negativo a positivo varias semanas después de la visita. Ambos exploraron las cuevas por un período de alrededor de hora y media y usaron mascarillas de papel la mayor parte del tiempo.

Recientemente, la Dra. Torres de Blasini ha logrado cultivar el *Histoplasma capsulatum* de la Cueva Los Panes, de Utuado.

**Discusión—** La evidencia que hemos presentado indica que la histoplasmosis es común en Puerto Rico. La tasa de infección entre estudiantes de medicina de Puerto Rico nos hace pensar que una tercera parte de los niños adquieren la infección antes de llegar a los 21 años. En la mayoría de los casos esta infección pasa desapercibida o produce el cuadro de una fiebre de origen desconocido de poca duración o síntomas respiratorios parecidos a los de una influenza o pulmonía viral. Es importante distinguir la histoplasmosis de tuberculosis y no hacer un diagnóstico de esta enfermedad por cambios radiográficos solamente. En toda persona en la que se sospecha tuberculosis, niño o adulto, debe hacerse una prue-

TABLA II — OBSERVACIONES EN LOS EXCURSIONISTAS ALREDEDOR DEL 4to MES DESPUES DE LA VISITA A LAS CUEVAS DE AGUAS BUENAS

Caso N.º	Edad	Histo-plasmina	Resultado de pruebas intracutáneas en mm.			Manifestaciones clínicas	Radiografía de torax	Infiltración lóbulos sup. der.	Neumonitis y Eritema Nudosa	Fijación de Complemento			Aglutinación de latex
			Battey	PPD-S	00					Blastomicosis	Histo-plasmina	Histoplasmosis (fase de levadura)	
1	15	17	00	00	Infiltración lóbulo sup. der.	Neumonitis y Eritema Nudosa	1:32	Neg	1:16	1:16	1:16	1:32	
2	15	19	00	00	Probable calcificación hiliar	Ninguna	1:8	1:8	1:8	1:16	1:16	1:64	
3	16	12	07	00	Probable calcificación hiliar	Débil, sin ánimo	1:16	1:8	1:8	1:16	1:16	1:16	
4	16	16	04	00	Aumento trama hilar y probable calcificación; calcificaciones en 3er y 5to interespacio anterior del lado derecho	Catarro, Catarro, Catarro	Neg	Neg	Neg	Neg	Neg	Neg	
5	15	16	00	00	Negativa	Ninguna	Neg	Neg	Neg	Neg	Neg	Neg	
6	16	10	00	00	Negativa	Ninguna	Neg	Neg	Neg	Neg	Neg	Neg	
7	18	18	02	00	Probable calcificación hiliar	Ninguna	Neg	1:16	1:16	1:16	1:16	1:8	
8	17	14	06	00	Probable calcificación hiliar	Ninguna	1:8	1:16	1:16	1:16	1:16	1:8	
9	17	15	03	00	Probable calcificación hiliar	Ninguna	1:8	1:16	1:16	1:32	1:32	1:8	
10	15	15	06	00	Aumento trama hiliar	Ninguna	Neg	Neg	Neg	No se hizo	No se hizo	No se hizo	
11	14	16	06	00	Probable calcificación hiliar y de la base derecha	Neumonitis	1:8	1:8	1:8	1:16	1:16	1:8	
12	15	00	No se hizo	—	—	Ninguna	Neg	Neg	Neg	No se hizo	No se hizo	No se hizo	
13	?	10	04	00	Negativa	Ninguna	—	—	—	—	—	—	
14	21	14	00	00	Negativa	Ninguna	Neg	Neg	Neg	Neg	Neg	1:8	

ba de tuberculina, y si ésta es negativa, debe investigarse el enfermo para histoplasmosis. La histoplasmosis simula todos los cuadros clínicos que produce la tuberculosis desde meningitis hasta lesiones cavitarias apicales pulmonares crónicas. Una calcificación pulmonar no debe interpretarse radiográficamente como un tubérculo de Gohn a menos que se haya hecho una tuberculina y ésta haya sido positiva. El diagnóstico correcto de histoplasmosis diseminada es indispensable, ya que el amfotericin B por la vía intravenosa puede salvarle la vida al enfermo.<sup>8</sup>

Histoplasmosis pulmonar contraída en exploraciones de cuevas ha sido descrita por varios autores. Un brote parecido al que hemos descrito fue informado desde Venezuela en el 1957.<sup>9</sup> Se trataba de un grupo de estudiantes y profesores espeleólogos que adquirieron la infección en las Cuevas de Barquisimeto. La evidencia que tenemos hasta la fecha indica que en Puerto Rico las Cuevas de Aguas Buenas y las cuevas Los Panes de Utuado son importante fuente de infección, aunque es probable que otras cuevas aún no estudiadas alberguen el hongo.

**Resumen y conclusiones—** La histoplasmosis es una micosis sistémica causada por el hongo *Histoplasma capsulatum*. El suelo es la fuente de contagio. Cerca de una tercera parte de los adultos en Puerto Rico han contraído la infección que, afortunadamente, en la mayoría de los casos es de evolución benigna. El cuadro clínico y radiográfico puede confundirse con el de tuberculosis, pulmonía primaria atípica, influenza y otras infecciones respiratorias parecidas. Las encuestas usando pruebas intracutáneas de histoplasmina han demostrado que la infección está ocurriendo en todas partes de Puerto Rico, tanto en áreas rurales como urbanas. Una investigación de un brote de histoplasmosis entre escolares excursionistas a las Cuevas de Aguas Buenas demostró que dichas cuevas son una importante fuente de contagio. Este hallazgo tiene importancia desde el punto de vista de salud pública, ya que grandes números de excursionistas, principalmente escolares, visitan estas cuevas. Asimismo, estas cuevas están rotuladas como refugios contra radiación por la Defensa Civil.

**Summary and Conclusions—** Histoplasmosis is a systemic mycosis due to the fungus *Histoplasma capsulatum*. The soil is the source of infection. About 1/3 of adults in Puerto Rico have had infection with histoplasmosis. Fortunately its course is usually benign. The clinical and roentgenographic picture can be confused with that of tuberculosis, primary atypical pneumonia, influenza and other similar respiratory infections. Surveys using intracutaneous histoplasmin have shown that the infection is taking place

throughout Puerto Rico, including rural and urban areas. An investigation of an outbreak of histoplasmosis among school children who visited the Aguas Buenas Caves revealed that these caves are an important source of infection. These findings have practical importance from the public health standpoint since the cases are visited by large number of excursionists and are designated as radiation shelters by the Civil Defense.

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## ELECTRICAL DEFIBRILLATION OF THE ATRIA

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Atrial fibrillation causes concern in rheumatic heart disease since it may carry a 30% risk of embolization and emboli may cause 10-20% of all deaths in such subjects.<sup>1</sup> Even if this were not sufficient reason to be concerned, it has been shown that tachycardia is associated with decreased cardiac efficiency<sup>2</sup> and that subjects with atrial fibrillation have a faster ventricular rate in response to exercise than they do after conversion to sinus rhythm.<sup>3</sup> Persistent atrial fibrillation, even in the absence of demonstrable heart disease, may lead to cardiomegaly and failure which is reversed by return to sinus rhythm.<sup>4</sup> There is adequate reason, then, to evaluate carefully the benefits and risks of therapeutic measures for atrial fibrillation.

Conversion of chronic atrial fibrillation to sinus rhythm with quinidine occurs in 50-55% of subjects with rheumatic mitral stenosis and 20-25% of those with mitral insufficiency.<sup>1</sup> This conversion of fibrillation to sinus rhythm by administration of quinidine, in one study increased cardiac output both during rest and after exercise by an average of 43% over control values.<sup>5</sup> It is not clear, however, how much of this result was due to the altered cardiac rhythm and how much was secondary to the hemodynamic effects of quinidine.<sup>5,6</sup> Furthermore quinidine in large doses decreases cardiac efficiency of experimental animals.<sup>7</sup> With the advent of closed-chest direct current defibrillation of the atria<sup>8</sup> a new source of data has become available. Unfortunately these data are not as clear as is desirable since electrical defibrillation is sufficiently unpleasant that general anesthesia is required in most instances and hence the effects of anesthesia as well as the change in cardiac rhythm must be evaluated. It is of considerable interest that a re-

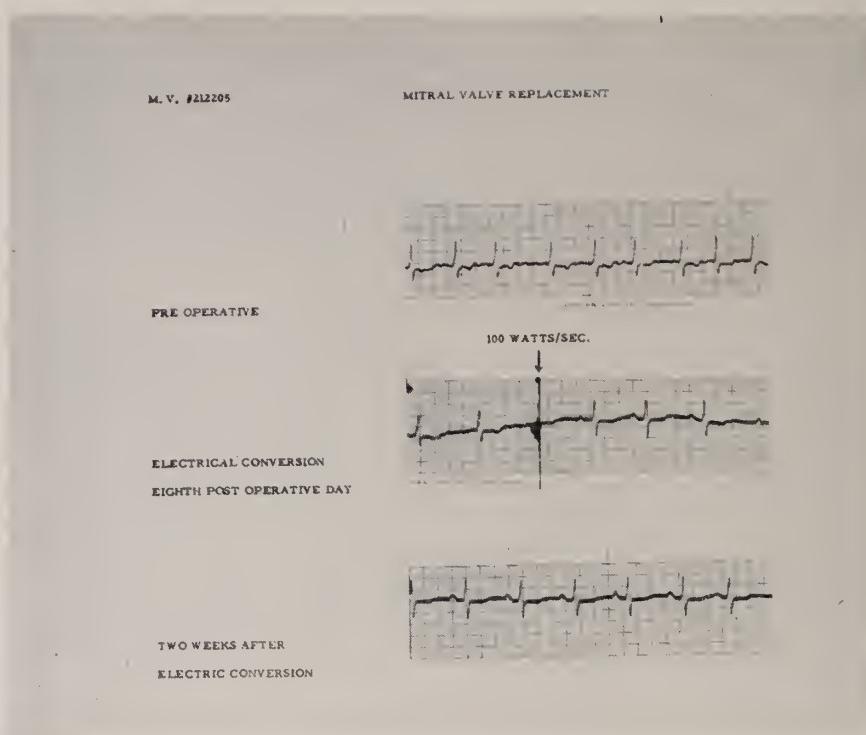
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cent report indicates no significant increase in cardiac output following conversion of subjects with atrial fibrillation to sinus rhythm by this method.<sup>9</sup> Some of the apparent discrepancy between the results with quinidine<sup>3</sup> and those with electrical defibrillation<sup>5</sup> may be clarified by considering that the effect of atrial fibrillation on cardiac output is rate-related. Thus when the ventricular rate is below 100 beats/minute, no significant change in output may occur on conversion of atrial fibrillation to normal sinus rhythm,<sup>3</sup> whereas at higher rates more change may be produced.

Another factor to consider is whether sinus rhythm persists in a significant number of instances after conversion, or whether it is difficult to prevent reversion to fibrillation, necessitating the indefinite use of a potentially toxic drugs.<sup>10,11</sup> The present report of our experience with electrical defibrillation of the atria during open heart surgery emphasizes the point of view that chronic atrial fibrillation usually occurs in a diseased heart and regardless of the method of defibrillation has a strong tendency to recur.

#### Material and methods

Fourteen patients are reported who had electrical countershock applied for atrial arrhythmias during mitral commissuro-

tomy or other cardiac surgery. Twelve of these had rheumatic heart disease with atrial fibrillation. In seven of these the atrial fibrillation had been present for some time prior to surgery (see Table 1.) whereas in five it developed for the first time during heart surgery. All of these patients received digitalis before surgery, and, except for case #3, have continued it since operation. One of the "chronic fibrillators" had taken quinidine continuously but ineffectively before operation.

The other two patients, had congenital heart disease. One of these developed atrial fibrillation while at surgery whereas the other developed supraventricular arrhythmia after open heart surgery and was treated medically for three days before electrical countershock was carried out in the operating room. Defibrillation was carried out during cardiac surgery in the traditional fashion utilizing the Burdick A. C. Defibrillator. The voltage and duration of the shock required are indicated in Table I. The electrocardiogram, systemic arterial and central venous pressures were recorded on the Gilson Direct-Writing Polygraph during the procedure and the diagnoses of both atrial fibrillation and return to sinus rhythm were made utilizing the information obtained from these recordings as well as direct viewing of the heart. The patients were followed post-operatively in the hospital and subsequently in the outpatient clinic.

#### RESULTS

All 14 patients were converted to sinus rhythm in the operating room by alternating current electrical shock. In four of the subjects (Cases #8, 10, 11 and 12) with rheumatic heart disease (42%) atrial fibrillation recurred during the ensuing minutes to hours before they had returned to the ward from the operating room. In three patients (Case #6, 7 and 9) atrial fibrillation recurred 1 or 2 days after surgery. In case #5, who developed fibrillation during surgery for the first time and whose fibrillation recurred after electrical defibrillation, later developed sinus rhythm spontaneously. In four cases where fibrillation developed during surgery, the follow-up visits to date reveal the electrical defibrillation was effective. Thus the seven "chronic fibrillators" reverted to chronic fibrillation, whereas the five who developed atrial fibrillation during surgery now have normal sinus rhythm.

Of the two patients with congenital heart disease who had electrical defibrillation of the atria, the one who first developed atrial fibrillation during surgery (Case #13), has sustained sinus rhythm. The other (Case #14) had resection of an infundibular pulmonic stenosis and four days later developed atrial flutter with

TABLE I. — DATA ON PATIENTS TREATED BY ELECTRICAL COUNTERSHOCK FOR ATRIAL ARRHYTHMIAS

Patient age in Yrs., Sex	Duration of Disease, Treatment	Diagnosis of AF to Treatment	Lesions	Surgery, By Pass minutes	Date & Dose of Shock (volts-secs. duration)	Rhythm Leaving OR	Drugs Post-Op	Comment Rhythm last Follow-up
1) R. M. 37 Yrs. Female	4 Years D	No	MS, MI	P. V. 120	4-16-63 300x0. 15 300x0. 15	NSR (2nd shock)	D	AF first in OR Sustained NSR (18 days)
2) C. D. 48 Yrs. Female	10 Years D	No	MS, MI	M. C. 61	9-22-61 150 x 0. 15	NSR	D	AF first in OR Sustained NSR (1.5 Yrs.)
3) G. W. 36 Yrs. Female	7 Years D	No	MS	M. C. 72	10-13-61 100 x 0. 15	NSR	none	AF first in OR Sustained NSR (1 Yr.)
4) L. H. 38 Yrs. Female	10 Years D	No	MS, MI and AI	M. C. 64	9-29-61 150 x 0. 15	NSR	D	AF first in OR Sustained NSR (13 months)
5) J. B. 32 Yrs. Male	22 Years D	No	MS	M. C. 90	10-11-62 250 x 0. 15	AF	D	AF first in OR, converted. Recurred OR. Spontaneous NSR on ward. Sustained NSR (5 months)
6) L. W. 35 Yrs. Female	8 Years D	6 months	MS	M. C. 54	1-10-63 100 x 0. 15	NSR	D Q	AF for 6 months, recurred 2 days post-op, remained in spite of quinidine.
7) L. F. 39 Yrs. Male	5 Years D	1 year	MS, MI	M. C. 56	1-17-63 100 x 0. 15	NSR	D P	AF for 1 year, recurred 1 day post-op, present since.
8) V. G. 48 Yrs. Female	2 Years D	1 year	MS (sub- valvular), MI, AI.	M. C. 42	4-11-63 250 x 0. 15	AF	D	AF for 1 year, recurred in OR (20 seconds), present since.

TABLE I — (CONTINUED)

Patient	Duration Age in Yrs., Sex	Diagnosis of AF to Treatment	Lesions	Surgery, By Pass minutes	Rhythm Leaving OR	Drugs Post-Op	Comment Rhythm last Follow-up
9) C. G. 30 Yrs. Female	21 Years D, P*	1 year MS, MI and AI	M. C. 45 and 58	5-23-63 100 x 0. 15	NSR	D	AF for 1 year, recurred 24 hours post-op, present since.
10) F. S. 51 Yrs. Female	25 Years D	5 Years MS, MI and AI	M. C. 82	10-27-61 150 x 0. 15	AF	D P*	AF for 5 years, recurred in OR ("few minutes"), present since.
11) R. M. 33 Yrs. Male	7 Years D, Q	7 Years MS, MI and AI	M. C. 61	9-7-61 not recorded	AF	D	AF for 7 years, recurred in OR (15 minutes), present since.
12) L. L. 57 Yrs. Female	10 Years D, P*	9 Years MS, MI	M. C. 43	3-28-63 200 x 0. 15 250 x 0. 15	AF	D	AF for 9 years, recurred in OR ("few beats"), present since.
13) E. H. 39 Yrs. Male	ASD VSD	Closure ASD & VSD 70		7-26-60 110 x 0. 1	SR		
14) J. L. 18 Yrs. Female	Inf. Pulm. Sten.		Removal Infundib. Stenosis 103	10-30-60 220 x 0. 5 220 x 1. 0 (manually 3 times)	A Flutter	D	Expired (Surgery 10-26-60)
	OR AF NSR D Q	Operating Room Atrial Fibrillation Normal Sinus Rhythm Digitalis Quinidine		P' MS MI AI M. C.	Diuretics Mitral Stenosis Mitral Insufficiency Aortic Insufficiency Mitral Commissurotomy	P. V. ASD VSD Int. St.	Prosthetic Valve Atrial Septal Defect Ventricular Septal Defect Infundibular Stenosis of the Right Ventricle

a rapid ventricular rate. All efforts at medical therapy failed and on the third day of arrhythmia, because of clinical deterioration, she was taken to the operating room for definitive correction of her arrhythmia. Ventricular fibrillation was produced by a preliminary trial at conversion with intravenous acetyl choline. Following thoracotomy, defibrillation and conversion to sinus rhythm was accomplished by the A. C. defibrillator. However, the supraventricular tachycardia recurred prior to return to the ward and the patient died the night after electrical countershock therapy.

#### DISCUSSION

An ideal method for conversion of atrial fibrillation to sinus rhythm should not only convert, but prevent recurrence of the arrhythmia. Not only would retreatment be avoided then, but the current danger of embolization accompanying a changing rhythm.<sup>1</sup> Such a transient event as electrical depolarization of the heart, although immediately effective in reverting the arrhythmia to sinus rhythm can not be expected to prevent its recurrence. In the present series, we have obtained sustained sinus rhythm in all cases when atrial fibrillation developed at operation for the first time. Similarly, in the subject with congenital heart disease who developed the arrhythmia at surgery, electroshock was successful and gave a sustained normal sinus rhythm. It would seem that when the precipitating circumstance is transient and has passed, electrical defibrillation may give a lasting result. Since considerable improvement in clinical status may be produced by electrical defibrillation of the atria when fibrillation arises acutely during surgery, this improvement alone may justify electrical defibrillation under certain circumstances without regard for its long range effect. This is particularly true since defibrillation of the atria can be accomplished with acceptably low electrical discharges.<sup>13</sup>

The major problem then, seems to concern patients with chronic atrial fibrillation who are not only more difficult to convert to sinus rhythm but also more prone to revert to fibrillation.<sup>10</sup> In the present series none of the seven "chronic fibrillators" sustained normal sinus rhythm after successful conversion by electroshock. It was hoped that if sufficient correction of the pathologic state which precipitated the arrhythmia was achieved by surgical intervention the fibrillation would not recur. In retrospect this seems to have been an unreasonable hope since, as far as cardiac rhythm is concerned, the long range results have been unrewarding, even though marked improvement in cardiac function did result. Our present findings agree with those of other

investigators<sup>16,17,18</sup> in that there was a high rate of success in conversion of atrial fibrillation to sinus rhythm by the use of electric shock (90%). This required that in some patients the shock be repeated; so that there has been always a greater number of shocks than there were patients. In some "refractory" cases from two to six shocks have been used.<sup>16</sup>

When maintenance of conversion of fibrillation is studied the results are poorer and the figures for patients remaining in sinus rhythm drop to 40-50%, when followed for 3 to 9 months.<sup>16,17,18</sup> These patients are those who have had atrial fibrillation of 1 to 3 years duration, giant left atrium or uncorrected mitral stenosis or insufficiency. This lower rate of permanent conversion occurred even though the patients in the above series were maintained on adequate maintenance doses of quinidine. In "refractory" cases, even maximally tolerated doses of the drug would not maintain sinus rhythm.<sup>16</sup> Thus it appears that for some patients with atrial fibrillation even a combination of several shocks and adequate quinidine maintenance is ineffective in producing or maintaining sinus rhythm.

It seems reasonable to assume that atrial fibrillation occurs in rheumatic heart disease as a manifestation of the underlying atrial dilatation and hypertrophy, valvular disease, myocardial fibrosis and other changes.<sup>14</sup> With adequate therapy and compensation, modification of the pathologic physiology undoubtedly occurs, but much of the underlying pathologic anatomy is likely to remain.<sup>14,15</sup> Thus it would appear probable that once the disease process has gone far enough to produce sustained atrial fibrillation it is unlikely that any transient form of therapy will produce a sustained change in rhythm. This thesis is supported by the results of the present series, as well as that in the previous report where only 8 of 21 subjects sustained sinus rhythm after electrical defibrillation of the atria.<sup>9</sup> The total risk of traditional medical therapy then must be weighed against the total risk in the "new regimen" of induction of anesthesia, closed chest electrical defibrillation and subsequent sustained drug therapy.<sup>11</sup>

The decision probably should not be made lightly to undertake anesthesia and transthoracic electrical depolarization of the heart, when the chances are considerable that the arrhythmia will be difficult to convert to sinus rhythm or the maintain converted if the method is successful. Auricular fibrillation of over 2 years duration, a giant left atrium, or severe uncorrected mitral stenosis or insufficiency will undoubtedly limit the success of the procedure. If these patients have been already refractory to quinidine therapy or allergic to its use or if quinidine therapy can not

be adequately maintained after conversion the procedure is clearly contraindicated.

#### SUMMARY

1—Twelve patients with rheumatic heart disease who had atrial fibrillation were defibrillated by an alternating current electrical defibrillator in the operating room while undergoing mitral commissurotomy.

Two patients with congenital heart disease who developed atrial arrhythmia and had defibrillation are also included.

2—This defibrillation was accomplished with electrical discharges which are well within the safe range as far as the heart is concerned.

3—Those subjects who developed atrial fibrillation for the first time during operation have sustained normal sinus rhythm. In those that had the arrhythmia prior to surgery it reappeared either during operation or within two days thereafter.

4—In established atrial fibrillation the underlying pathological process in the heart is sufficiently advanced that maintenance of normal sinus rhythm after conversion is apt to be difficult and will require continued medical therapy.

5—Since electrical defibrillation does not seem to influence the tendency for the arrhythmia to recur, one of the major problems in treatment of chronic atrial fibrillation remains. Quinidine therapy cannot be discarded, as although electrical defibrillation may be effective at conversion, it may not be expected to prevent recurrence in chronic fibrillation if the factors responsible for the arrhythmia remain.

#### RESUMEN

La fibrilación auricular es causa de preocupación en la enfermedad reumática del corazón puesto que conlleva un riesgo de embolización que puede ocasionar la muerte. Además de esto, puede producir cardiomegalia y disminución de la eficiencia cardíaca. Por estas razones deben evaluarse cuidadosamente los métodos para su tratamiento.

Entre los métodos con que se cuenta actualmente para su tratamiento está el uso de la quinidina y el shock con corriente eléctrica. En la enfermedad reumática del corazón acompañada de fibrilación auricular debe preocuparnos no solamente si se puede convertir la arritmia a ritmo sinusal sino también que esta conversión sea duradera.

El presente informe presenta nuestra experiencia con la defibrilación eléctrica del atrio durante cirugía abierta al corazón.

Enfatiza el punto de vista de que la fibrilación auricular crónica en general ocurre en corazones enfermos y no importa el método que se use para convertirla tiene gran tendencia a recurrir.

En este estudio presentamos 14 pacientes con fibrilación auricular a los que se le aplicó shock eléctrico durante una comisurotomía u otra cirugía cardiovascular.

Doce de ellos tenían enfermedad reumática y los otros dos, enfermedad congénita. Todos los 14 pacientes obtuvieron conversión de la arritmia a ritmo sinusal mediante el uso de shock con corriente eléctrica alterna.

Los pacientes con fibrilación atrial crónica no mantuvieron la conversión. Los que desarrollaron fibrilación en la sala de operaciones, tanto reumáticos como congénitos, sí mantuvieron la conversión hasta el momento de este informe.

Este estudio sugiere que cuando existe fibrilación auricular crónica los cambios patológicos en el corazón harán el mantenimiento de ritmo sinusal muy difícil. Por esta razón no puede eliminarse el tratamiento con quinidina y se considera que el control de la fibrilación crónica aún persiste como un problema terapéutico.

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# ADVANCES IN DIAGNOSIS BY NEWER LABORATORY PROCEDURES\*

F. WILLIAM SUNDERMAN, M.D., Ph.D.\*\*

The advances in diagnosis owing to newer chemical procedures have been so rapid, varied and complex that to cover the topic fully would be a Herculean task requiring a number of hours. As a consequence, in organizing our material, we propose to present only a resume of some of the biochemical procedures that have evolved during recent years and which, in our opinion, are proving to be helpful aids in diagnosis.

The selected procedures will be considered in relation to the chemical categories given on Table 1. It should be recognized at the outset of any consideration of laboratory procedures that the majority are not pathognomonic of any specific disease. Most procedures serve merely as blocks in the foundations upon which clinical diagnoses are established.

## I. Nitrogenous Components

### A. Identification of Abnormal Hemoglobins and Hemoglobin Derivatives

Rapid advances have been made in the characterization of hemoglobinopathies. The hemoglobinopathies may be classified into two general categories: 1) those associated with genetically related abnormalities of the hemoglobin molecule particularly in relation to its structural configuration; and 2) those in which the hemoglobin is presumably normal but has undergone a chemical change to form a hemoglobin derivative. Common examples of the former are S Hemoglobin in sickle-cell anemia and Hemoglobin C disease; examples of the latter are methemoglobinemia and sulfhemoglobinemia.

Ever since Pauling and his associates in 1949<sup>26</sup> demonstrated that the sickling phenomenon seen in **Sickle-cell disease** was due to the presence of hemoglobin with abnormal physico-chemical characteristics, many studies have been undertaken in the differentiation of a number of other abnormal hemoglobin. Study of the chemical composition of these abnormal hemoglobins indicate that the amino acids, the iron content and other basic components in the molecule do not differ greatly from each other. The main dif-

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ference in these hemoglobins has been shown to be in the structural configurations of the hemoglobin molecule.

The hemoglobin molecule is composed of 2 alpha and 2 beta chains. The alpha chains each have 142 amino acids and the beta chains each have 146. The sequence of the various amino acids in these chains has now been established. Deviations in the normal

TABLE 1.

## ADVANCES IN DIAGNOSIS BY NEWER LABORATORY PROCEDURES

## I. NITROGENOUS COMPONENTS

- A. Abnormal Hemoglobins and Hemoglobin Derivatives: Myoglobinuria (Familial, Periodic Idiopathic and Haff's Disease)
- B. Blood Ammonia: Hepatic Coma; Cardiac Failure; Uremia
- C. Serotonin: Carcinoid Tumors
- D. Amino Acid Fractionations: Phenylketonuria; Arginine-succinic abnormality; Hartnup's Syndrome; Oast-house Syndrome; Maple-syrup Syndrome; DeToni-DeBre-Fanconi Syndrome.
- E. Paper Electrophoresis of the Serum Proteins: Aid in diagnosis of many pathologic conditions, specifically: Agammaglobulinemia A-albuminemia, and Alpha-3 globulinemia.

## II. CARBOHYDRATE COMPONENTS

- A. Glucose Oxidase Procedures
- B. Chromatographic Procedures: Galactosemia; Sucrosuria (Moncrieff's Syndrome); Fructosuria with Hypoglycemia.

## III. LIPID COMPONENTS

- A. Fractionation of Serum Lipids: Free Fatty Acids (FFA, UFA, NEFA) — Diabetes and Metabolic Disorders; Triglycerides (neutral fats) — idiopathic hyperlipidemia (Burger-Grutz); Phospholipids (lecithin, cephalins, sphingomyelins) — Niemann-Pick's Disease
- B. Lipoproteins: Atherosclerosis and A-beta globulinemia

## IV. HORMONES AND THEIR METABOLITES

- A. Catecholamines : For the diagnosis of Pheochromocytoma
- B. Vanilmandelic acid
- C. 17-OH Corticosteroids for estimations of adrenal cortical function
- D. Aldosterone for diagnosis of Primary and Secondary Aldosteronism

## V. ENZYMES

- A. Transaminases (SGOT & SGPT): Myocardial infarction and liver disease
- B. Lactic Acid Dehydrogenase: Injury to cardiac and skeletal muscle, Leukemia, Lymphomas and liver disease
- C. Cholinesterase: Detection of exposure to organic phosphorus compounds and "nerve" war gases
- D. Characterization of Acid Phosphatases: Differentiation between Gaucher's Disease and prostatic malignancy

## VI. MINERALS

- A. Advances related to iodine in serum
- B. Sweat test as an aid in diagnosis of fibrocystic disease of pancreas
- C. Metabolism of trace metals

sequence may lead to important alterations as, for example, sensitivity sulfonamide therapy.<sup>12,18</sup>

The methods of differentiation of the abnormal hemoglobins are based essentially on differences in electrophoretic mobilities, solubilities in salt solutions and resistance to alkali denaturation. The study of hemoglobin variants is especially helpful in the diagnosis of the various hemolytic anemias. Important refinements in diagnosis and treatment may be expected in future years from the study of abnormal hemoglobins.

Mention may be made at this time of the renewed interest in the detection of myoglobin in the urine as an aid in the diagnosis of both familial<sup>17</sup> and idiopathic paroxysmal myoglobinuria.<sup>27</sup> Primary idiopathic paroxysmal myoglobinuria is a relatively rare disease of ominous prognosis characterized by muscle necrosis and the release of myoglobin into the urine. An epidemic type of myoglobinuria (so called Haff's disease) has been described<sup>6</sup> and is apparently caused by the ingestion of certain fish in north sea waters. Myoglobinuria may also be observed after extensive injury to skeletal muscle. The diagnosis of myoglobinuria is dependent upon the differential solubility and the dialyzability of myoglobin as well as the spectroscopic identification of the absorption bands of myoglobin.

The lower molecular weight of myoglobin (17,500) is consistent with its greater solubility in comparison to hemoglobin with a molecular weight of 68,000. For example, at 80 percent saturation with ammonium sulfate, hemoglobin is completely precipitated; myoglobin is not.

## B. Blood Ammonia

Reliable methods have been developed within the past decade for the measurement of blood ammonia which have been helpful in delineating the role played by this nitrogen component in various pathologic states. It has been shown that ammonium salts administered to experimental animals are capable of provoking episodes of hepatic coma. This has focused attention upon the role of the increased concentration of blood ammonia in hepatic coma. Under normal conditions, the ability of the liver to remove ammonia, principally by the formation of urea, is so great that ammonia is virtually absent in the peripheral blood.

Ammonia is produced in the body in reactions involving the metabolism of proteins and amino acids, especially glutamic acid. Glutamic acid appears to be the only essential amino acid that is utilized directly by the brain. Glutamic acid may unite with ammonia to form glutamine. Therefore, any gross excess of ammo-

nia in the blood may remove the glutamic acid that is required for cerebral metabolism. Coma associated with increased concentrations of ammonia in the blood has been ascribed to the binding of glutamic acid by ammonia.<sup>4,5</sup>

In addition to hepatic coma, elevations of blood ammonia have been correlated with the development of mental symptoms associated with chronic cardiac failure. The work of Bessman<sup>5</sup> has demonstrated that the concentration of blood ammonia is increased as a result of chronic passive congestion of the liver and failure to remove ammonia from the portal system.<sup>22</sup>

### C. Serotonin (5-hydroxytryptamine)

Serotonin is a nitrogen component formed by the chromaffin cells of the gastro-intestinal tract. It may be mentioned that serotonin is absorbed on the blood platelets, although it is not formed by them. The tumors arising from the chromaffin cells of the gastro-intestinal tract are referred to as "carcinoid" tumors. Such tumors, particularly if they have metastasized to the liver, are associated with increased concentrations of serotonin in the circulating blood. Such increases produce a syndrome of flushing, diarrhea, asthma and valvular disease of the right heart.

TABLE 2

INFLUENCE OF FOODS, TOBACCO, DRUGS AND PATHOLOGIC  
CONDITIONS UPON THE URINARY EXCRETION OF  
5-HYDROXYINDOLE ACETIC ACID

INCREASED

<i>Foods and Tobacco</i>		<i>Drugs</i>	<i>Pathologic Conditions</i>
Bananas	Avocados	Tryptophan	Malignant Carcinoid Tumors of Intestines, Bronchi & Gonads
Plantain	Tomatoes	Reserpine (variable)	Tropical and Non-tropical Sprue
Walnuts	Eggplant	Mephenesin	Whipple's Lipodystrophy
Currents	Pineapples	Methocarbamol	Pancreatic Carcinoma
Plums	Gooseberries	Glyceryl Guiacolate	Hepatolenticular Degeneration
Melons	Smoking Tobacco	Phenolsulfonphthalein	Myocardial Infarction
		Pyridium	Migraine Headache
			Post-operative Period

DECREASED

<i>Drugs</i>	<i>Pathologic Conditions</i>
Iproniazid	Phenylketonuria
Phenothiazines	Hartnup's Disease
Benzylserotonin	Pre-eclamptic Toxemia
Homogentisic Acid	Radical Intestinal Resection

A useful procedure for the measurement of a metabolite of serotonin, i.e. 5-hydroxy-3-indole acetic acid, has been developed by Udenfriend and coworkers.<sup>46</sup> This measurement is a useful aid in establishing the diagnosis of "carcinoid". The normal excretion of 5-hydroxy-3-indole acetic acid is less than 7 mg per 24 hours. Values in excess of 15 mg per 24 hours are usually encountered in carcinoid.

With increasing utilization of the measurements of 5-hydroxy-3-indole acetic acid, it has been recognized that a large number of foods, pharmacologic agents and pathologic conditions are associated with the urinary excretion of this compound. These sources of artefactual elevations are summarized on Table 2. It might be mentioned that increased urinary excretion of 5-hydroxy-3-indole acetic acid has been consistently found in a patient with Wilson's Disease.<sup>36</sup>

#### D. Amino Acid Fractionations

Abnormal patterns in the excretion of amino acids in the urine have been described in a wide variety of pathologic conditions. Important advances have been made in the methodology of amino acid separations. Practically all of the recent method involve techniques of paper and column chromatography and electrophoresis.

In the past few years there has been a constant flow of articles describing metabolic errors of amino acid metabolism asso-

TABLE 3  
METABOLIC ERRORS OF AMINO ACID METABOLISM

Phenylketonuria	Defect is apparently the missing enzyme in conversion of phenylalanine to tyrosine
Arginine-Succinic acid Syndrome	Increased urinary excretion of arginine and succinic acid
Hartnup's Syndrome	Block is located in the conversion of tryptophan to nicotinic acid
Oast-house Syndrome (kiln where hops are dried)	Increased excretion of amino acids
Maple Syrup Syndrome	Increased urinary excretion of valine, leucine and isoleucine
DeToni-DeBre-Fanconi Syndrome	Dwarfism, Vitamin D-resistant rickets, amino-aciduria

ciated with mental defects. The rapid advances in this field have been due largely to the advances in chromatographic analysis by which separations of amino acids can be made on relatively small amounts of blood and urine that can be obtained from infants. A few examples of metabolic errors are listed in Table 3.

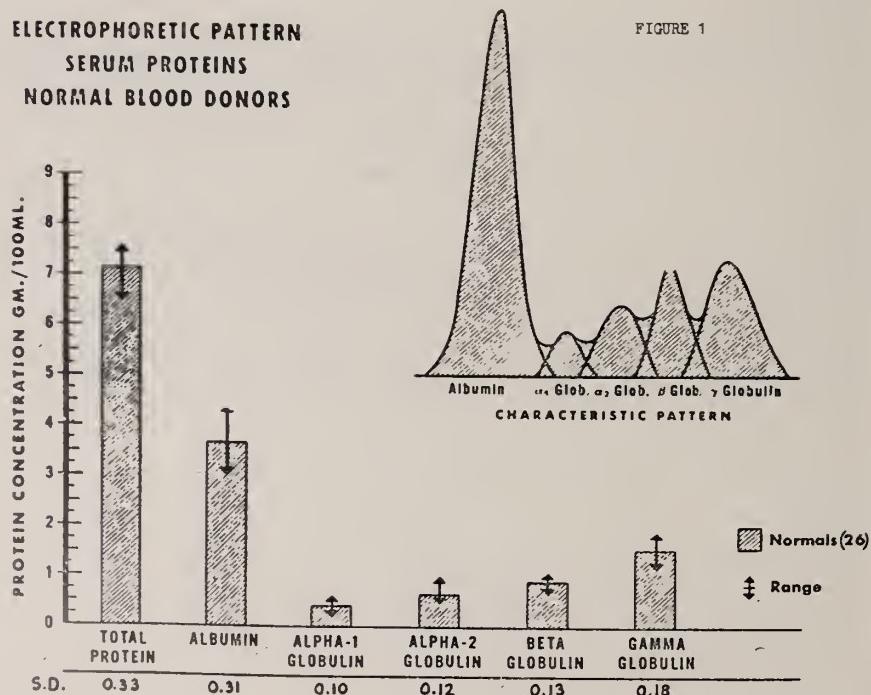
#### E. Paper Electrophoresis of the Serum Proteins.

Separation of the serum proteins into albumin and globulin fractions has become an important clinical aid, owing to the recent development of rapid and dependable methods for paper electrophoresis. In addition to aiding in the diagnosis of many pathologic conditions, the separation of serum proteins is essential for the diagnosis of certain clinical entities: agammaglobulinemia, analbuminemia, bisalbuminemia and alpha-3-globulin syndrome. The electrophoretic patterns of the serum proteins in hepatic cirrhosis, nephrosis Boecks sarcoid, multiple myeloma, Waldenstrom's macroglobulinemia and lymphatic and myelogenous leukemia, while not pathognomonic, nevertheless, are very distinctive.

Within the past five years we have studied the electrophoretograms of the serum proteins from approximately 4000 patients who suffered from a wide variety of pathologic conditions encountered in general hospital practice. At this time it may be of interest to present a few of our electrophoretic patterns.

ELECTROPHORETIC PATTERN  
SERUM PROTEINS  
NORMAL BLOOD DONORS

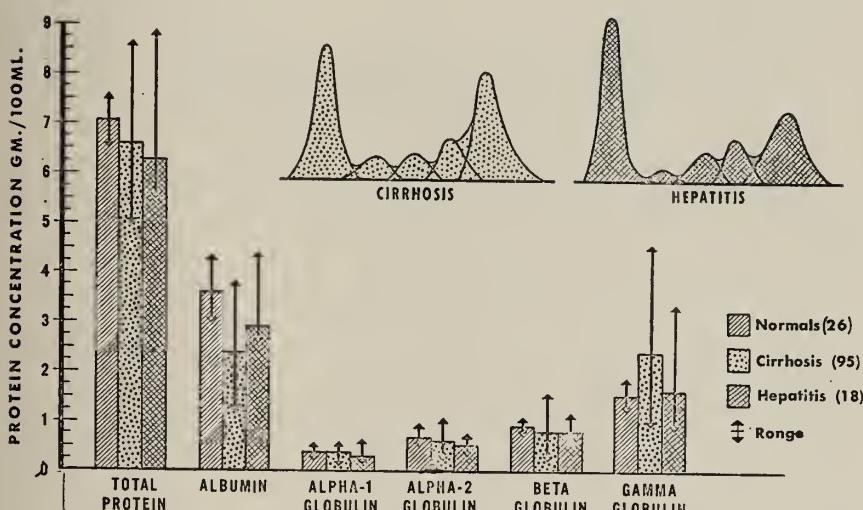
FIGURE 1



The data of the electrophoretograms obtained from twenty-six normal blood donors are summarized on Figure 1. The mean concentration of total proteins for the normal group was 7.14 gm per 100 ml, with a standard deviation of  $\pm 0.33$  gm per 100 ml. The concentrations of the protein fractions are shown in the bar graphs and the extreme range of values is indicated by the arrows. The means electrophoretic pattern is also portrayed.

Our series of electrophoretograms included 95 cases of hepatic cirrhosis and 18 of viral hepatitis. A summary of the findings for hepatic cirrhosis is shown on Figure 2. A characteristic pat-

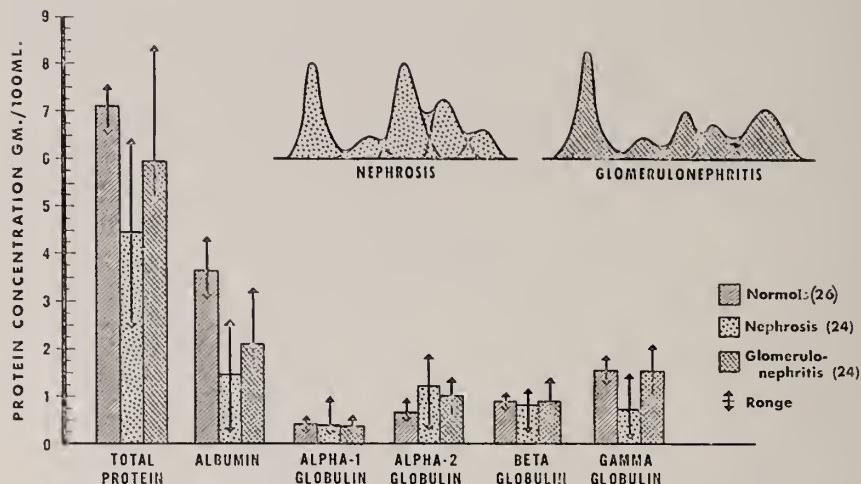
FIGURE 2.  
HEPATIC CIRRHOSIS AND VIRAL HEPATITIS



tern for hepatic cirrhosis is portrayed in the upper left portion of the figure. The mean values for total protein and for each of the protein fractions in cirrhosis are portrayed by stippled columns in the middle. Viral hepatitis is portrayed by the hatched columns on the right. These are compared with the hatched columns representing normal values (on the left); the highest and the lowest values for each group are represented by the arrow heads.

It will be seen that the mean concentration for total protein and the mean concentration for albumin are decreased in our series of patients with cirrhosis. It will also be seen that the mean concentration of gamma globulin is increased above the normal. It is noteworthy that the concentrations of the alpha and beta globulins in our patients with portal cirrhosis and hepatitis do not differ significantly from the normal group.

FIGURE 3.  
NEPHROTIC SYNDROME AND CHRONIC GLOMERULONEPHRITIS



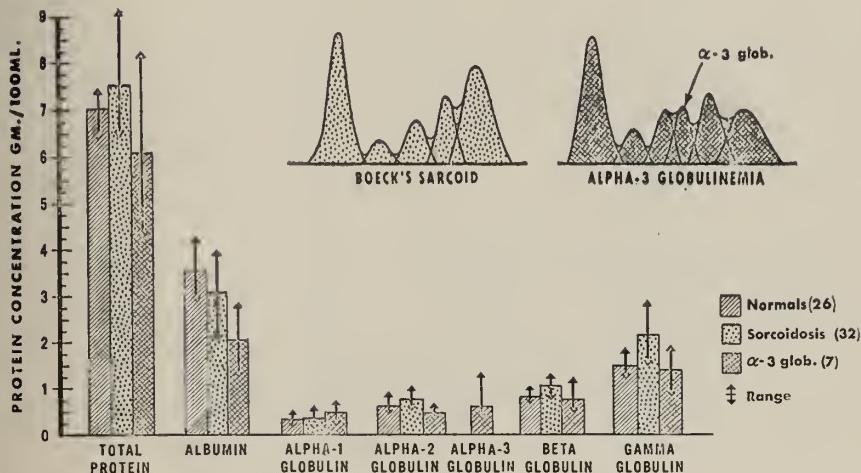
On Figure 3 is portrayed our analysis of the protein fractions in nephrosis and chronic glomerulonephritis not in the nephrotic state.

A unique and characteristic pattern was obtained in all of our 24 patients with nephrosis. The mean value of each of the protein fractions was significantly altered. All of the fractions excepting alpha-2 globulin were decreased. Alpha-2 globulin, on the other hand, was increased in all cases, the mean value being twice the normal mean concentration. It should be emphasized that all of our cases had marked reduction in gamma globulin, the mean concentration was one third that of the normal and indeed approached the values observed in "hypogammaglobulinemia". Data from our 24 patients with chronic glomerulonephritis not in the nephrotic syndrome are also shown in Figure 3. As will be seen, the albumin concentration is decreased although not as pronounced as in the nephrotic syndrome. The total globulin concentration tends to be within the normal limits although there is a slight but significant increase in the alpha-2 fraction.

To recapitulate, in our nephritic patients, the mean values for albumin were decreased whereas the mean values for alpha-2 globulin were increased. The most striking changes were found in the nephrotic syndrome, particularly in reference to the observed hypogammaglobulinemia.

A unique and characteristic mean pattern was observed in 32 patients suffering from Boeck's sarcoid. It will be seen on Figure 4 that the mean concentration of total protein was significantly

FIGURE 4.  
BOECK'S SARCOID AND ALPHA-3 GLOBULINEMIA



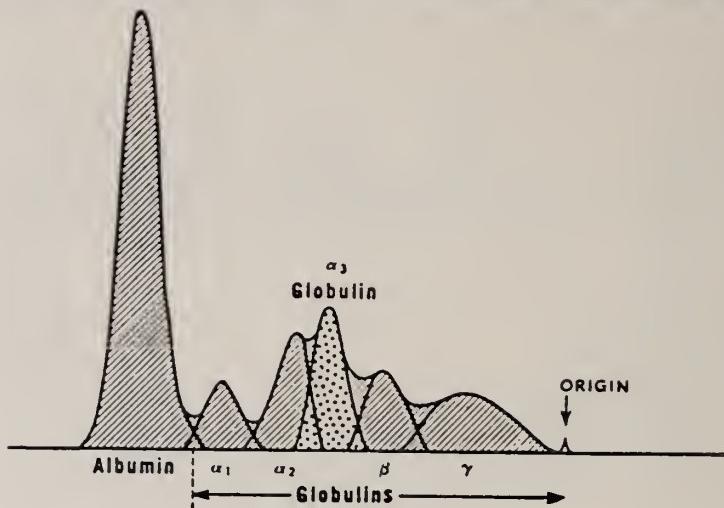
increased, and that this increase is due essentially to increases in the alpha-2, beta and gamma globulins. The albumin concentration tended to be decreased. It has been particularly noteworthy that the globulin fractions portray a steplike progression from alpha-2 through the gamma fractions. The configuration of the pattern, as shown on the figure, has been observed in practically all of our patients, and we refer to it as the "sarcoid steps".

Ever since we have undertaken electrophoretic studies our attention has been focused upon an abnormal component that is occasionally encountered migrating between alpha-2 and beta globulin. We prefer to refer to this component as alpha-3 globulin. On Figure 5 is portrayed an electrophoretogram to illustrate the pattern of alpha-3 globulinemia.

In our series of electrophoretograms alpha-3 globulin was observed in concentrations greater than 0.3 gm per 100 ml in the sera from 26 patients who suffered from a variety of neoplastic diseases, infections, and metabolic disturbances. In seven of these patients alpha-3 globulinemia was associated with a distinctive clinical picture which included **chronic myalgia, arthralgia, anemia, emaciation, fever, dermatitis and pleurisy**. No etiologic agent or specific pathologic lesion could be identified. In this group of patients the age incidence, symptomatology, physical and laboratory findings and clinical courses bore such striking similarities that we believe they warrant special classification.<sup>33,35</sup>

In no disease have the electrophoretic patterns been studied more intensively than in **multiple myeloma**. A number of years ago it had been shown that patients with multiple myeloma had

FIGURE 5.  
ELECTROPHORETIC PATTERN ALPHA-3 GLOBULINEMIA

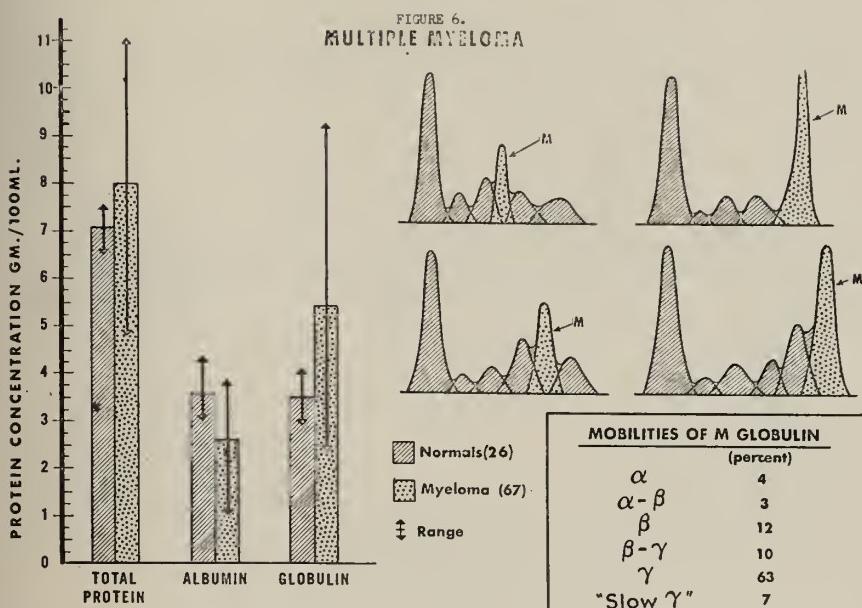


an abnormal protein circulating in the serum which is believed to be derived from abnormal plasma cells. Martin<sup>23</sup> compared the electrophoretic and ultracentrifugal mobilities of the abnormal serum globulin in a patient with multiple myeloma to those of the globulin extracted from the patient's tumor tissue at autopsy. He obtained similar mobility values in serum and tumor tissue and suggested that the abnormal protein in multiple myeloma arises from the tumor cells.

On Figure 6 are shown some of the different types of electrophoretic patterns found in 99 cases of multiple myeloma in our series. The abnormal protein, which Gutman<sup>16</sup> termed the "M" globulin is designated by the stippled pattern. In 4 of our 99 cases the "M" globulin was at the alpha position; in 3 between the alpha-2 and beta position, as shown in the upper left corner of the figure. In 12 cases the "M" globulin was at the beta position and in 10 between the beta and gamma position as shown in the left corner. In 63 of our cases, a sharply defined peak was obtained at the gamma position (upper right corner and in 7 cases, shown in the right lower corner, the "M" globulin had a mobility less than the gamma fraction. This has been called the "slow gamma" globulin.

All the evidence suggests that the "M" protein in multiple myeloma is a separate entity having a well defined mobility in any given case, and is frequently characterized in paper electrophoresis by a narrow peak.

Owing to the varying mobility of the "M" globulin, our statis-



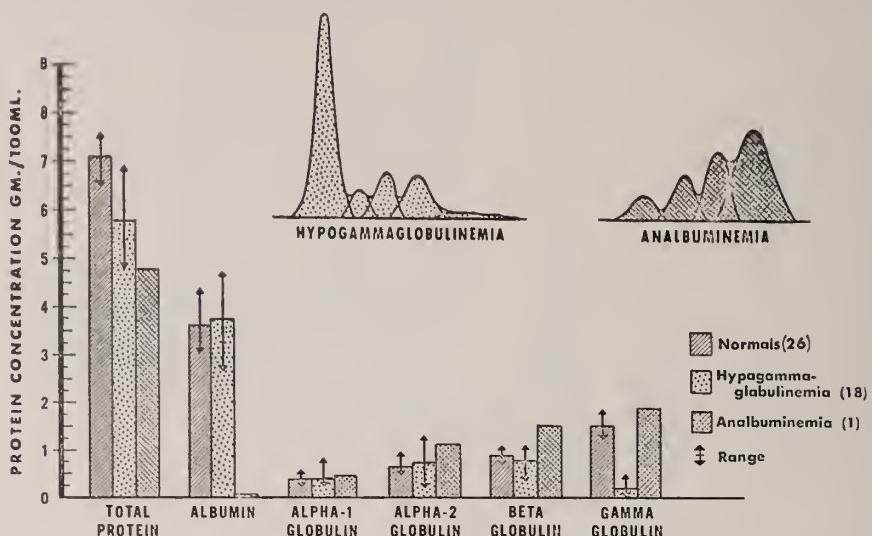
tical evaluation of the serum fractions in multiple myeloma has been restricted to albumin and total globulins. It will be seen that the mean concentration of serum albumin is significantly decreased, and that of total globulins significantly elevated.

The syndrome "agammaglobulinemia", or preferably, "hypogammaglobulinemia" has been widely recognized since it was first described by Bruton in 1952.<sup>7</sup> Two clinical types have been described, — the congenital and acquired. The congenital type occurs as a sex-linked recessive trait, most frequently affecting male infants; the acquired type affects adults of both sexes. The condition is characterized by repeated infections, mostly of the respiratory system, marked diminution in the concentration of gamma globulin, and inability to elaborate antibodies. In paper electrophoresis, a complete absence of protein at the gamma position is rarely observed. This is due to the fact that traces of the more rapidly migrating proteins remain at the gamma globulin position and are included in the calculation.

Eighteen patients with typical hypogammaglobulinemia are included in our series. It will be seen on Figure 7 that gamma globulin alone is significantly altered, — the decrease in total protein being due to the diminished gamma globulin.

There is another rare congenital disease, analbuminemia, that is characterized by an absence or marked diminution of albumin in the serum. Bennhold and associates<sup>3</sup> in Marburg first described this congenital anomaly in a pair of siblings in 1954. Since then a

FIGURE 7.  
HYPOGAMMAGLOBULINEMIA AND ANALBUMINEMIA



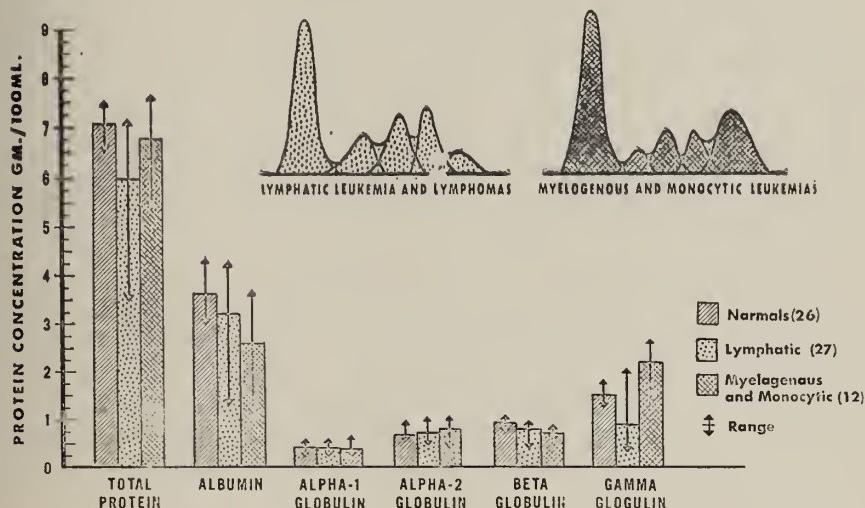
number of cases have been found. We have had an opportunity to study one case. The most striking feature of analbuminemia is the relative paucity of symptoms. Usually mild edema has been noted which is relieved by the administration of albumin.

The deficiency of serum albumin in analbuminemia can be attributed to failure of albumin production and not to an exaggerated rate of removal of albumin from the circulation. Hypercholesterolemia usually accompanies analbuminemia. Administration of albumin in the amount of 25 grams per week is attended by a sense of well-being and the correction of the hypercholesterolemia. Prolonged hypercholesterolemia may contribute to the development of premature atherosclerosis.

Striking differences are observed in the electrophoretograms in the serums of patients suffering from lymphatic and myelogenous leucemia (Figure 8). In 27 patients with lymphatic leucemia the concentration of gamma globulin was found to be markedly decreased. The low concentrations of gamma globulin in lymphatic leucemia are in marked contrast to the increased concentrations of gamma globulin observed in the majority of our 12 patients with myelogenous and monocytic leucemias. This difference in the concentration of gamma globulin is proving to be a useful diagnostic aid.

The mean pattern obtained in 14 patients with Hodgkin's disease (Figure 9) is similar to that observed in myelogenous and monocytic leucemias with the additional findings that alpha-1 and

FIGURE 8.  
LYMPHATIC LEUKEMIA AND LYMPHOMAS; MYELOGENOUS AND MONOCYTIC LEUKEMIAS

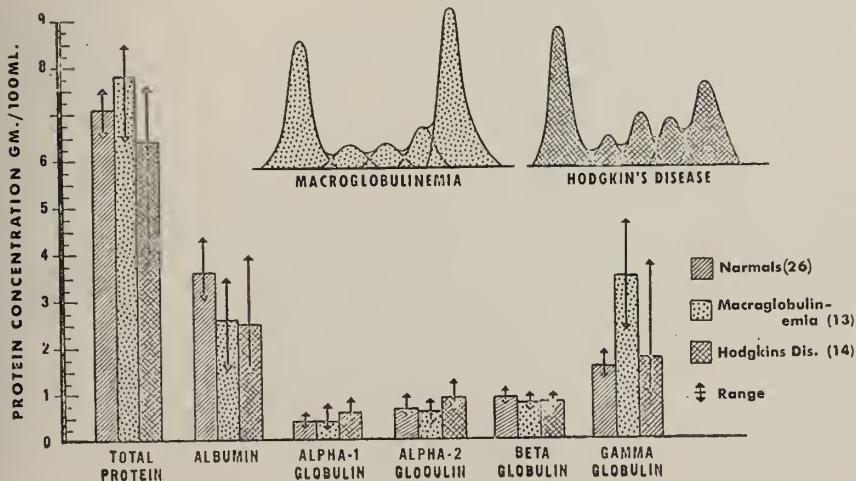


alpha-2 globulins are elevated and the concentration of albumin is decreased.

The mean pattern in 13 cases of macroglobulinemia (Figure 9) revealed markedly increased concentrations of gamma globulin and diminished concentrations of serum albumin.

So much for a brief resume' of Protein Electrophoresis.

FIGURE 9.  
MACROGLOBULINEMIA AND HODGKIN'S DISEASE



## II. Carbohydrate Components

Advances in diagnosis are being achieved as a result of the newer glucose-oxidase methods developed for the measurement of blood glucose. Glucose-oxidase methods yield values of greater specificity, accuracy and reliability than the copper and ferri-cyanide reduction methods in current clinical use. A new glucose-oxidase procedure recently developed in our laboratory<sup>34</sup> yields values 9 percent lower than by the usual copper reduction method and 7 percent lower than by the Autoanalyzer ferri-cyanide reduction procedure.

The increased specificity of glucose measurements by glucose-oxidase procedures and chromatographic technics enables the clinician to make refinements in the diagnosis of abnormalities of carbohydrate metabolism. The diagnoses of galactosemia, sucrosuria and fructosuria are a few examples of refinements in diagnosis that have been elucidated in recent years by these newer laboratory techniques.

### A. Galactosemia

Galactosemia is a disease of early life which becomes evident when the infant fails to thrive and develops an intolerance to milk. Blood from these infants contains galactose. The most serious cases develop mental retardation, jaundice, cataracts, hepatic enlargement, diarrhea and lethargy.

Galactosemia is no longer a clinical curiosity. Schwarz<sup>29</sup> has indicated that within the span of a few years approximately 50 cases had been diagnosed in Great Britain (some of them post mortem). Since treatment with a galactose-free diet offers promising results if started early, every effort should be made to establish the diagnoses. It is important that the siblings of known galactosemic parents be tested at birth.

Clinically, the diagnosis is usually established by galactose tolerance tests and the presence of galactose in the urine. Isselbacher, et al in 1956<sup>19</sup> demonstrated that the metabolic block in Galactosemia is in the deficiency of **galactose-1-phosphate uridyl transferase** in the erythrocytes. A number of methods have been devised to measure this deficiency. Most of the methods are laborious<sup>31</sup> and not adaptable for routine use; however, within the past few years, Schwarz<sup>30</sup> developed a simplified qualitative test by which a diagnosis can apparently be made within a few hours of birth.

### B. Sucrosuria (Moncrieff's Syndrome)

Moncrieff and Wilkinson<sup>24,25</sup> described a syndrome associated with mental retardation and hiatal hernia associated with the excretion of sucrose in the urine. The diagnosis is made by the chromatographic identification of sucrose in the urine.

### C. Fructosuria

In 1959, Froesch<sup>13</sup> described a familial disease in which the ingestion of fructose produces a high concentration of fructose in the blood associated with concomitant diminutions in blood glucose and symptoms of hypoglycemia. Copper and ferri-cyanide reduction methods fail to distinguish between fructose and glucose in the blood of patients with this abnormality. However, by the use of glucose-oxidase methods and chromatography the diagnosis of the fructosuria anomaly can readily be made.

## III. Lipids

No field of clinical chemistry is so neglected by the clinician as that of lipid metabolism. For most clinicians, laboratory evaluation of lipid metabolism is limited to the determination of serum cholesterol and cholesterol esters. Lacking reliable data for the normal concentrations of serum cholesterol with respect to age and sex, the clinician finds it difficult to interpret even the results of this analysis.

### A. Free Fatty Acids

The current nomenclature is somewhat confusing. The terms FFA, UFA, and NEFA are all used to indicate the same moiety. They refer to free fatty acids, unesterified fatty acids and nonesterified fatty acids. We prefer to use the term "free fatty acids." FFA represents a small but highly significant fraction of the serum lipids. It is currently believed that free fatty acids represent the lipid fraction which is immediately available to meet the energy demands of the body. Gordon<sup>14</sup> and Laurell<sup>21</sup> have shown that measurements of free fatty acids are proving useful in the study of patients with diabetes. In the treatment of diabetic acidosis the concentration of free fatty acids appears to return to the normal range more rapidly than blood glucose or CO<sub>2</sub>.<sup>14</sup>

### B. Triglycerides or Neutral Fats

The measurement of this moiety is finding usefulness in establishing the diagnosis of idiopathic hyperlipidemia (Burger-

Grutz Syndrome) and in various tolerance tests to measure fat absorption. The triglycerides constitute the preponderant lipid constituent of adipose tissue.

### C. Phospholipids

The phospholipids are the primary lipids in non-adipose tissue. They play a structural role in cellular membranes and are especially abundant in nerve and liver tissues. Serum phospholipids are synthesized and metabolized almost entirely in the liver and the concentration of phospholipids in serum is proving to be useful as an index of liver function. The phospholipids may be subdivided into the lecithins, cephalins and sphingomyelins. The abnormal lipid in Niemann Pick's disease is now classed as sphingomyelin.

### D. Lipoproteins.

Newer techniques with paper electrophoresis in which the lipoproteins are stained with the dye —Fat Red 7B— held promise for routine use in the clinical laboratory; however, recently the results have been disappointing. Calculations of the ratio of beta-lipoprotein to alpha-lipoprotein appears to be useful in classifying individuals as to the degree of atherosclerosis. With the accumulation of data from lipoprotein fractionations, it is to be expected that significant correlations regarding atherosclerosis may be forthcoming.

A new syndrome of a-beta lipoproteinemia was described by Salt and his colleagues<sup>28</sup> in England a few years ago. Already we have learned of the detection of two additional cases in this country. This condition apparently arises from an inborn error of metabolism in which the primary defect is the inability of an individual to form the beta-lipoprotein molecule. The diagnosis should be suspected in any patient suffering from steatorrhea associated with very low concentrations of serum cholesterol and the presence of spiked red cells called "acanthocytes". In one patient, the concentration of serum cholesterol was 10 mg per 100 ml. In the case reported by Salt and coworkers<sup>28</sup> the concentration of cholesterol was 22 mg per 100 ml. No other disease entity with which we are familiar is associated with such amazingly low concentrations of serum cholesterol. In a-beta-lipoproteinemia, separation of the lipoproteins in the serum reveals a complete absence of the beta-lipoprotein fraction.

#### IV. Hormones and their Metabolites

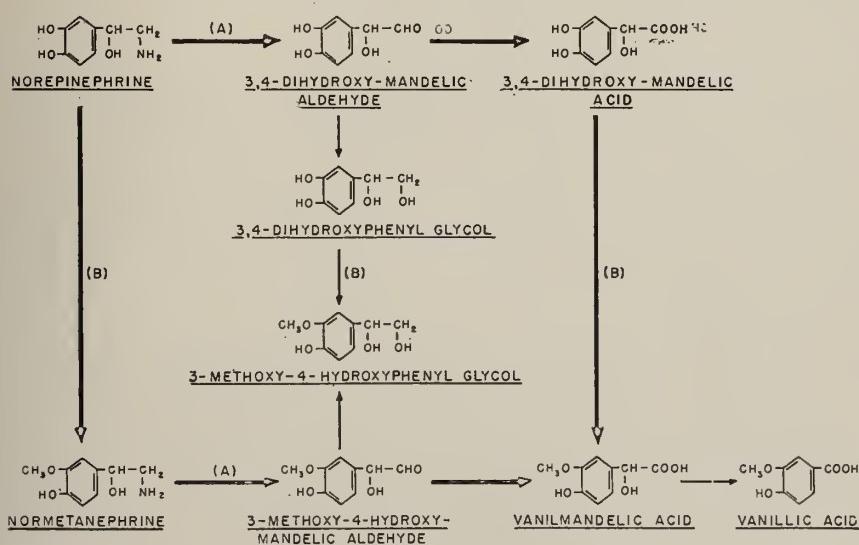
##### A. Catecholamines and their Urinary Metabolites

Biochemical methods for the diagnosis of pheochromocytoma have been a subject of investigation in our laboratories for several years.<sup>37</sup> Although emphasis was originally placed upon measurements of urinary catecholamines, more recently our interest has been directed to the urinary metabolites of the catecholamines, and particularly to 3-methoxy-4-hydroxymandelic acid (vanilmandelic acid). In 1957, Armstrong, McMillan, and Shaw<sup>1</sup> reported vanilmandelic acid to be a major urinary metabolite of norepinephrine, and noted the urinary excretion of vanilmandelic acid to be increased in patients with pheochromocytoma. Subsequent investigations have confirmed these observations and have stimulated interest in the clinical application of measurements of vanilmandelic acid to the diagnosis of pheochromocytoma.

For the purpose of orientation, the major pathways of norepinephrine metabolism have been summarized in Figure 10. Norepinephrine may undergo *o*-methylation by action of catechol-*O*-methyl transferase to form normetanephrine.<sup>2</sup> A portion of the normetanephrine is excreted in the urine either in unconjugated form or as a sulfate or glucuronide conjugate. A second portion of normetanephrine is deaminated by action of mono-amine oxidase to yield 3-methoxy-4-hydroxymandelic aldehyde. A small

##### PATHWAYS OF NOREPINEPHRINE METABOLISM

FIGURE 10.



(A) = Mono-Amine Oxidase; (B) = Catechol-O-Methyl Transferase

fraction of this intermediate is reduced to 3-methoxy-4-hydroxyphenylglycol, which is excreted in the urine, but the major fraction is oxidized to vanilmandelic acid. As an alternative pathway, norepinephrine may be deaminated to yield 3, 4-dihydroxymandelic aldehyde. This intermediate may be reduced to 3, 4-dihydroxyphenylglycol or oxidized to 3, 4-dihydroxymandelic acid. A portion of 3, 4-dihydroxymandelic acid appears in the urine, but the major portion undergoes *o*-methylation to yield vanilmandelic acid. Vanilmandelic acid is largely excreted in the urine without metabolic alteration, but a fraction is oxidized to vanillic acid. The metabolic pathways of epinephrine are analogous to those of norepinephrine, leading to the excretion of metanephrine and the deaminated metabolites which are illustrated in Figure 10.<sup>2,8</sup>

Seventeen patients with pheochromocytoma have been encountered in our study<sup>37</sup> of 1489 hypertensive patients. In each instance the diagnosis of pheochromocytoma was supported by the clinical findings, by positive regitine or histamine tests, and by elevated excretion of urinary vanilmandelic acid. Thirteen of the pheochromocytomas in our series were observed in adults and four in children. In 14 of the 17 patients, the pheochromocytomas were benign and in 3 they were malignant. The excretion of vanilmandelic acid in the adult patients ranged from 15 to 250 mg per 14 hours. Our normal range for adults is 0.7 to 6.8 mg per 24 hours. In the 4 children with pheochromocytoma, the excretions of vanilmandelic acid were generally lower than in the adult group,—ranging from 11 to 21 mg per 14 hours.

### B. Corticosteroids

Precise determination of the steroid hormones are becoming increasingly important in the diagnosis of adrenocortical and gonadal dysfunction. Within the past few years, methods have been developed for measuring corticosteroid metabolites (the so-called Porter-Silber chromogens). These measurements serve as useful guides for the estimation of adrenal cortical function.

### C. Aldosterone

This is the adrenal hormone which is believed to be primarily responsible for the control of electrolyte metabolism. The chromatographic procedures for the separation of aldosterone are exceptionally arduous and the procedure is by no means a routine type of analysis. In our opinion the usefulness of the measurement as a diagnostic aid in hospital practice appears to be diminishing.

Clinical interest in aldosteronism centers about two types: primary aldosteronism (Conn's syndrome) and secondary aldosteronism.

Primary aldosteronism manifests itself by an elevated excretion of aldosterone in the urine and normal levels of 17-hydroxycorticosteroids and 17-ketosteroids, alkalosis, excessive excretion of potassium, diminished excretion of sodium, moderate elevations of serum sodium and decreased concentrations of serum potassium. The symptoms that develop clinically are severe muscle weakness, periodic or intermittent episodes of paralysis, tetany and hypertension. The patients complain of excessive thirst and polyuria. The syndrome is characterized by an absence of edema.

Secondary aldosteronism is characterized by an increased excretion of aldosterone in the presence of cardiac and renal failure with edema. The amount of aldosterone excreted in patients with cardiac and renal failure may be correlated with the degree of edema. When the edema diminishes, the output of aldosterone decreases.

## V. Enzymes

### A. Transaminase

Approximately nine years ago the determination of serum glutamic oxaloacetic transaminase was introduced into clinical medicine, primarily as a useful index of myocardial necrosis.<sup>20</sup> Although a number of transaminase activities have been demonstrated in human serum, the two serum transaminases currently of clinical importance are serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT). Both serum enzymes may be measured chromatographically, spectrophotometrically and colorimetrically.

Serum glutamic oxaloacetic transaminase is present in cardiac muscle in high concentration. After myocardial infarction the concentration of enzyme in the serum rises to a peak in 12 to 24 hours and then gradually returns to normal in 3 to 5 days. Tremendous elevations of SGOT may also be observed in various liver diseases. The elevations in liver disease usually persist for a much longer period of time than those in myocardial infarction.

A few years ago attention became focused upon the difference in distribution of SGOT and SGPT in human heart tissue and in human liver tissue. Both heart and liver tissues contain about 150,000 units of SGOT per gram of tissue. However, heart tissue contains only about 7000 units of SGPT per gram whereas liver tissue contains 44,000 units per gram. This relationship explains

the high concentration of SGOT observed after myocardial infarction and the normal level of SGPT in this condition.

It also became apparent that the concentration of SGPT in acute hepatitis was usually increased earlier and remained elevated a little longer than SGOT.

### B. Lactic Acid Dehydrogenase

The measurement of lactic dehydrogenase is proving to be of considerable clinical importance. This enzyme is more widely distributed than the transaminases and elevations of lactic dehydrogenase are observed in a variety of pathologic states including leukemia, lymphomas, metastases, carcinomatosis, as well as injury to the cardiac and skeletal muscle. The relative simplicity of measurement helps to compensate for the relative lack of specificity of increase in this enzyme.

### C. Cholinesterase

The primary usefulness in the measurement of serum cholinesterase is in the detection of exposure to organic phosphates and fluorophosphates present in insecticides and miticides and to "nerve" war gases. Tetraethyl pyrophosphate and parathion are the best known examples of organic phosphorus insecticides that are anticholinesterases.

Any marked depression in the cholinesterase activities of either plasma or red blood cells that is coincidental to the exposure of organic phosphorus compounds, should be interpreted as resulting from the absorption of toxic materials. With the prevalent use of insecticides, clinicians should be on the alert for the detection of organic phosphorus intoxication. The usual initial symptoms include weakness, blurred vision, tingling sensations and gastrointestinal complaints. These symptoms become marked when the serum cholinesterase is decreased to 50 percent of the normal value. Workers with insecticides should be tested routinely and removed from their work if activity is decreased to 75 percent of their normal cholinesterase activity.

### D. Phosphatase

The observation that serum acid phosphatase may have different properties in different diseases has proved to be important in the differentiation of Gaucher's disease and prostatic malignancy. In both conditions the concentrations of serum acid phosphatase are elevated. In Gaucher's disease the acid phosphatase is not inhibited by tartrate; in prostatic malignancy, it is.

## VI. Minerals

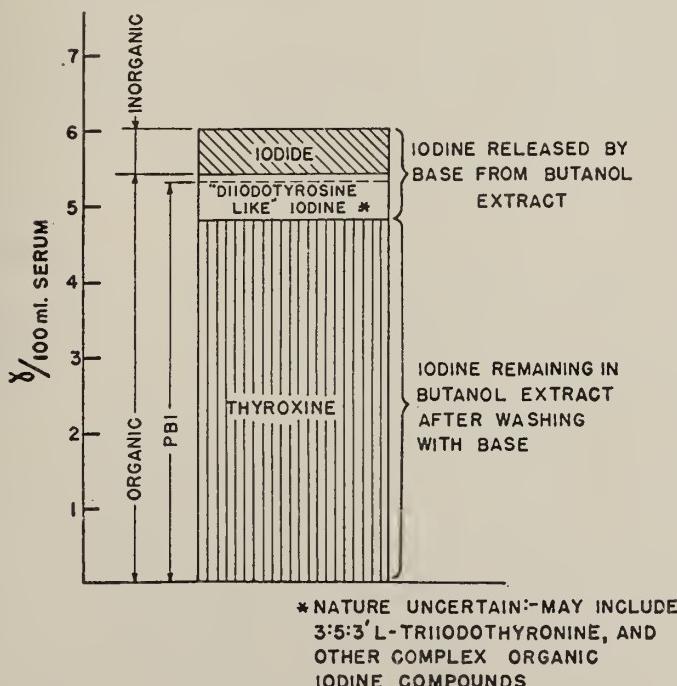
### A. Protein Bound Iodine

No measurement in clinical medicine in recent years has received greater emphasis as a diagnostic aid than that of PBI in serum. It has now become well established that this measurement reflects the concentration of circulating thyroid hormone.

The normal partition of iodine in serum is portrayed on Figure 11. The organic iodine in serum constitutes approximately 90 percent of the total iodine, the remaining 10 percent is chiefly in the form of inorganic iodide. Although most of the organic iodine is bound to protein, there is a small portion that is unbound and has physiologic significance. This fraction includes free thyroxine in very low concentration.

Almost all of the iodine in serum may be extracted with butanol and, by subsequent re-extraction with alkali, may be separated into two fractions. The larger fraction remains in the butanol; it constitutes about 81 percent of the total iodine and consists almost entirely of thyroxin. The smaller fraction, which is in the alkali extract, contains inorganic iodide and organic com-

**FIGURE 11.  
PARTITION OF SERUM IODINE**



pounds long believed to be similar to mono-and di-iodotyrosine and called by Trevorrow<sup>45</sup> "the di-iodotyrosine-like" fraction. Gross and Pitt-Rivers<sup>15</sup> succeeded in demonstrating 3-5-3' tri-iodothyronine in this fraction. Wynn<sup>47</sup> recently re-investigated this "di-iodotyrosine-like" fraction and failed to detect any mono- or di-iodothyroxine but succeeded in separating a compound, the chemical nature of which is not identified.

An important recent contribution to our knowledge of protein bound iodine has been the demonstration that at least three distinct fractions of the serum proteins are responsible for the binding of thyroxine. These three "thyroxine-binding proteins" (TBP) include: "thyroxine-binding globulin" (TBG), which has an electrophoretic mobility between alpha-1 and alpha-2 globulins; "thyroxine-binding albumin" (TBA); and "thyroxine-binding pre-albumin" (TBPA) which has an electrophoretic mobility approximately 20 percent faster than serum albumin. Several investigations suggest that the three thyroxin-binding proteins may be affected differently by various physiologic, pathologic and pharmacologic influences.

### Methods

The methodology of protein bound iodine will not be discussed at this time excepting to state that the measurement of this moiety in serum is not an easy analysis. Without the observance of quality control procedures, errors are apt to creep into the measurement. On Table 4 are listed the quality control procedures which are considered necessary to ensure dependable measurements.

TABLE 4

#### QUALITY CONTROL PROCEDURES FOR DEPENDABLE MEASUREMENTS OF PROTEIN BOUND IODINE

1. All unknown samples should be analyzed in duplicate with the measurement being repeated if the duplicates differ by more than  $\pm$  0.3 mcgm per 100 ml.
2. Daily measurements should be made on pooled control serums.
3. Measurements of the recovery of thyroxine added to serum should be undertaken periodically, preferably at weekly intervals.
4. Special procedures should be instituted to prevent cross contamination by high iodine containing seras.
5. New lots of reagents should be tested for the presence of contaminants.

FIGURE 12.

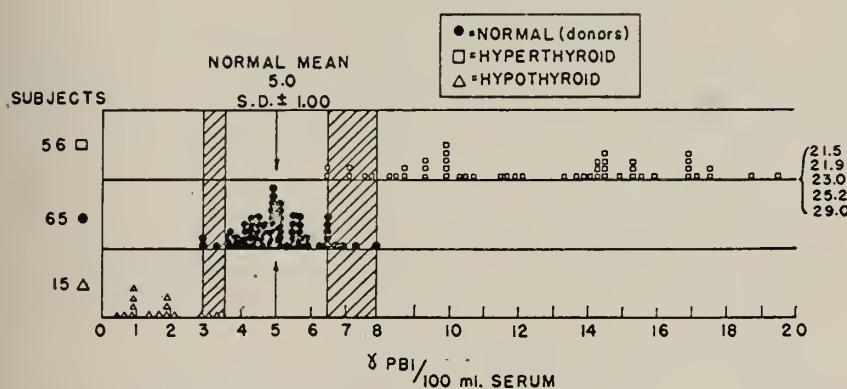


FIG. 12. Concentrations of protein-bound iodine in the serum of normal persons and of hyperthyroid and hypothyroid patients.

On Figure 12 are illustrated the concentrations of PBI in normal subjects and in carefully selected patients with definite clinical signs of hyper- and hypothyroidism. The mean normal value was 5.0 mcgm per 100 ml with a S.D. of  $\pm 1.0$ . In 56 hyperthyroid patients the concentration of PBI ranged from 6.5 to 29 mcgm per 100 ml and in the 15 hypothyroid patients the concentration ranged from 0.4 to 3.4 mcgm per 100 ml. The cross-hatched areas in the figure portray the overlappings of these values within the normal ranged.

For many years it has been recognized that abnormal concentrations of protein-bound iodine are encountered in various physiologic and pathologic states in which there are no clinical findings suggestive of hyper- or hypothyroidism (Table 5). Recent in-

TABLE 5  
PHYSIOLOGIC AND PATHOLOGIC ALTERATIONS IN PBI MEDIANATED  
BY CHANGES IN THYROXINE-BINDING PROTEINS

- |  |  |
|--|--|
| INCREASED                                      |  |
| Pregnancy (increased TBG; normal TBPA)         |  |
| Infancy (increased TBG)                        |  |
| Hepatitis (increased TBG)                      |  |
| Post-thyroidectomy (circulating thyroglobulin) |  |
| Idiopathic (? genetic) increase in TBG         |  |
| DECREASED                                      |  |
| Nephrosis (decreased TBA and TBG)              |  |
| Chronic, debilitating disease (decreased TBPA) |  |
| Idiopathic (? congenital) absence of TBG       |  |
| QUESTIONABLE                                   |  |
| Stress; Surgery; Fever; (decreased TBPA)       |  |
| Senescence (male)                              |  |

vestigations have indicated that these alterations may be mediated by changes in the thyroxine-binding proteins. As shown on the table, increased concentrations of PBI are encountered in pregnancy, infancy, infectious hepatitis and in the postoperative period following thyroidectomy. In addition there are certain individuals in whom increased concentrations of PBI appear to be secondary to an idiopathic, and possibly genetic increase in thyroxine-binding globulin (TBG).

Decreased concentrations of PBI are encountered in nephrosis, associated with decreased thyroxine-binding globulin, and in chronic, debilitating diseases, which may be associated with decreased thyroxine capacity of thyroxine-binding pre-albumin (TBPA). The variations of PBI induced by stress, fever, surgery and in the post-partum period have not been thoroughly evaluated.

### Influence of Medications upon PBI

Medications may cause depression in the PBI, either through pharmacologic or artefactitious mechanisms as summarized in Table 6. Among the pharmacologic causes of diminished concentration of PBI may be listed: inhibition of TSH production owing to triiodothyronine or cortisone and ACTH therapy; inhibition of thyroxine production, owing to anti-thyroid drugs such as propyl- and methylthiouracil; drug-induced decrease in thyroxine-binding globulin which follows methyltestosterone therapy, displacement of thyroxine from thyroxine-binding proteins, such as has been reported with dinitrophenol, salicylate, diphenylhydantoin (dilantin) and tetrachlorothyronine; and the unexplained depression of PBI caused by chlorpromazine and reserpine.

Artefactitious depression of PBI may be caused by mercurial diuretics as a result of inhibition of the final ceric-arsenite color reaction in the analysis of protein bound iodine.

As shown in Table 6, pharmacologic elevations of PBI may result from the administration of TSH, thyroxine, and estrogens such as diethyl-stilbestrol. In the latter instance, the elevation appears to be secondary to an increase in thyroxine-binding globulin.

Artefactitious increase in PBI may result from massive therapy with inorganic iodides and bromides. Such elevations may usually be obviated by repeated washings of the precipitated protein. Organic iodide, diiodohydroxyquinoline and iodochlorhydroxyquinoline, and iodinated albumin may also cause elevations. Of all of these agents, the ones which most frequently elude detection are the iodinated hydroxyquinolines, which are incorporated in vaginal suppositories used for the therapy of trichomonas infes-

TABLE 6  
INFLUENCE OF MEDICATIONS UPON SERUM PBI  
PHARMACOLOGIC DEPRESSION

1. Inhibition of TSH production: Triiodothyronine; cortisone and ACTH.
2. Inhibition of production of thyroxine: Propylthiouracil; methylthiouracil;  $I^{131}$  therapy.
3. Decrease in thyroxine-binding proteins: Methyltestosterone (decreased TBG).
4. Displacement of thyroxine from thyroxine-binding proteins: 2, 4-dinitrophenol, (TBPA); salicylate, (TBPA); diphenylhydantoin, (TBG); tetrachlorothyronine, (TBG & TBPA).
5. Mechanism undetermined: Chlorpromazine; reserpine.

ARTEFACTITIOUS DEPRESSION

1. Inhibition of Ce-As color reaction: Mercurial diuretics.

PHARMACOLOGIC ELEVATION

1. TSH stimulation of production and release of thyroxine.
2. Therapeutic administration of thyroxine.
3. Increase in thyroxine-binding proteins. Diethylstilbestrol (increased TBG).

ARTEFACTITIOUS ELEVATION

1. Inorganic iodides and bromides: KI; KBr; Lugol's solution, tincture of iodine.
2. Organic iodine compounds: Iodothiouracil (anti-thyroid); dithiazanine iodide (anti-helminthic); diiodo-and iodochlorhydroxyquinoline (antiamebics); iodinated albumin (plasma volume determination); roentgenologic contrast media (see Table 7).

tations. The use of "Floraquin" suppositories twice daily for one week by 7 subjects produced a mean increase of 3.9 mcgm per 100 ml in the concentration of PBI. Use of "Vioform" suppositories caused a significant elevation in 1 of 3 patients whom we tested.

It has come to be recognized that there is wide variability in the rate of excretion and metabolism of idionated compounds which are employed as roentgenologic contrast media (Table 7). Thus, in urography, increased values for PBI persist for 1 month after administration of "Urokon", but only for 4 days following use of "Hypaque". In cholecystography, the agent "Teridax" is metabolized at an extraordinarily slow rate. It has been estimated that 33 years may be required to bring the PBI to the true value. On the other hand, "Orabilex" and "Biligrafin" are metabolized and excreted within a relatively few weeks.

In bronchography, "Lipiodol" causes artefactitious increases in PBI which persist for 1 to 5 years, whereas the increases following use of "Bionosil" persist for only 5 months. In order to permit measurements of PBI as soon as possible after radiologic

TABLE 7  
ELEVATION OF PBI BY ROENTGENOGRAPHIC CONTRAST MEDIA

CONTRAST MEDIUM	DURATION OF ELEVATION
<i>Urography</i>	
1. "Urokon"	1 month
2. "Diiodrast"	2 weeks
3. "Pyelombrine"	2 weeks
4. "Hypaque"	4 days
<i>Cholecystography</i>	
1. "Teridax" ("Trilombrine")	Many years
2. "Priodax"	3-4 months
3. "Telepaque"	1-4 months
4. "Orabilex"	1-2 months
5. "Biligrafin"	3 weeks
<i>Bronchography, Myelography, etc.</i>	
1. "Lipiodol" (intrathecal) (bronchial) (oral)	5 years 1-5 years 1½ years
2. "Dionosil" (bronchial)	1½-5 months

studies, radiologists should be encouraged, wherever possible, to use the contrast media which are most rapidly metabolized or excreted.

#### B. Sweat Test for Fibrocystic Disease

The quantitative "sweat test", because of its inherent reliability, relative simplicity, and generally clear-cut results, has become the cornerstone of diagnosis of cystic fibrosis. This procedure introduced by Shwachman and others,<sup>32</sup> following the reports by Darling<sup>9</sup> and diSant'Agnese,<sup>10</sup> of uniquely elevated sodium and chloride concentrations in the sweat of 98 to 99 percent of the patients with cystic fibrosis of the pancreas, has found far wider acceptance and application than other biochemical procedures for the diagnosis of cystic fibrosis.

Dubowski<sup>11</sup> determined the concentrations of sodium and chloride in samples of sweat from 146 normal control subjects (8 weeks to 20 years of age) and in samples from 19 persons (14 months to 9 years of age) suffering from cystic fibrosis of the pancreas. The range of sodium concentrations in the sweat of the patients with cystic fibrosis ranged from 60 to 138 mEq per liter with a mean of 103.7 mEq with a S.D. of  $\pm$  18.2. In contrast, the range for the normal subjects was 5 to 65 mEq per liter with a mean of 26.6 mEq, S.D.  $\pm$  13.8. Normal sweat rarely contains

sodium and chloride in concentrations above 60 mEq per liter; the sweat of patients with cystic fibrosis are usually well above this value.

### C. Trace Metals

The metabolism of trace metals such as nickel, copper and cobalt are receiving intensive study. Nickel carbonyl, for example, is being used in many industrial operations and the measurement of nickel in urine is being used for the detection of exposure to the poisonous vapors of nickel carbonyl. The presence of nickel in urine has proved to be a more sensitive criterion for the detection of exposure than the appearance of acute symptoms.<sup>38,39,40,41,42,43</sup> The findings of copper retention and diminution in the concentration of ceruloplasmin (the copper-binding serum globulin) are helpful aids in establishing the diagnosis of Wilson's disease and in following the efficacy of therapy.<sup>44</sup>

In closing may we emphasize the need of furthering research in the conduct of our medical wards and clinical laboratories. It is our belief that probably the greatest single step in the progress of medical science was made when clinical observation was fortified by the experimental methods of the laboratory. This is a landmark in the progress of medicine that is frequently passed by without the realization of the struggles that were encountered along the way. The determination to keep extending the experimental approach to the bedside is one of our greatest obligations and tasks in the years to come.

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THE ACUTE ABDOMEN, A VIEW FROM THE X-RAY  
DEPARTMENT

Amongst all the X-ray examinations, the one of the acute abdomen can be the most troublesome. I am ready to admit that I often feel worried when the X-ray request states: "colicky pain, no B.M. for 48-hrs.; R.O. intestinal obstruction", or "Pancreatitis", or "Cholecystitis". The film may show no significant amount of gas or a great deal of gas; no fluid levels or definite fluid levels. In case of gas distention, usually the problem is where the gas is located. Although I have spent probably more time in studying the X-ray appearance of the acute abdomen than any other condition, I must confess that at times I find it difficult to differentiate a colonic loop from an ileal loop when they are equally gas-distended. One comes across sooner or later a radiologically "typical" case of small bowel obstruction which at exploration proves to be a pancreatitis or cholecystitis with a reflex ileus! Or, vice versa: a clinically clear-cut case of mechanical small bowel ileus which will show almost no gas in the film because the obstruction is high in the proximal jejunum and the patient happens to be a stoical individual, who fails to swallow air.

The interpretation of the film of the acute abdomen can be a frustrating experience and the radiologist is entitled to worry. The frustration is hardly sweetened when a few hours later, in drops the physician in charge of the patient and after having looked at the film for an entire second, will generously offer his X-ray interpretation: "Come on, this is a clear case of reflex ileus! What's your worry? There is no peristalsis, the amylase is 790", etc. As it happens, the X-ray report has already been sent to the ward; the radiologist is indelibly committed to his diagnostic impression: Mechanical small bowel obstruction... My point is this: if there is one situation in which "team work", so emphasized in every medical article, is absolutely necessary to arrive at the most probable diagnosis, it is in the "Acute Abdomen". If you, as a surgeon or internist, feel the need for an X-ray examination for your clinical diagnosis, it is your duty to come to the X-Ray Department, and discuss the case with the radiologist. This would possibly cut down significantly approximately 20% of the cases which are problems. Unfortunately, the exchange of ideas is rarely carried out and unfortunately, at times the X-ray examination is requested because it is part of the "good work-up" of the case. Sometimes, I wonder whether this also means "good medicine".

Oftentimes, vital clinical information is unwittingly withheld from the radiologist. The hurriedly scribbled X-ray request frequently fails to indicate such data as history of previous abdominal operation, character of pain, peristaltic activity, just to mention a few. It makes a world of difference between the X-ray diagnoses of obstruction and reflex ileus and the most dreaded of all, strangulation.

Can't we aim higher and stop playing the guessing game?

Of course it is impossible to cover this subject even superficially within the scope of an editorial, but I felt that emphasizing certain points in regard to the acute abdomen could improve our "team work". If the implied criticisms touch a few sensitive souls, I wish to quote from Plato in my defense:

"NOTHING SPOKEN OR WRITTEN IS OF ANY GREAT VALUE IF THE OBJECT IS MERELY TO BE BELIEVED, NOT TO BE CRITICIZED AND THUS TO LEARN MORE."

Laszlo Ehrlich, M.D.

## SECCION DE RESUMENES

**THE PATTERN OF HEARING AFTER ACUTE OTITIS MEDIA** (Patrones aurapéutica de la hepatitis lupoidea). Mackay I. R. M.D., Wood I. J. M.D.; The Clinical Research Unit of the Walter and Eliza Hall Institute of Medical Research, and the Royal Melbourne Hospital, Melbourne, Australia - GASTROENTEROLOGY 45:4 July 1963.

Los autores estudiaron la evolución y el resultado de la terapia durante un período de 10 años en 24 pacientes que sufrían de la condición que algunos autores reconocen con el nombre de hepatitis lupoidea. Esta entidad se define como una hepatitis crónica y progresiva con factor L.E. positivo.

Para el propósito del estudio, la terapia utilizada fué de una duración de 7 - 14 días. El tratamiento con esteroides (prednisona) fué de comienzo inicial o por incremento en la dosis de mantenimiento. La dosis promedio de prednisona fué de 60 mgs. También se utilizó la 6-mercaptopurina a dosis de 100-150 Mgs por día durante 10-14 días. La prueba con antibióticos incluyó la tetraciclina a dosis de 2 Gms diarios, durante 14 días. Con anterioridad al año 1956 la respuesta al tratamiento dependía de los valores de la bilirrubina sérica y más adelante se evaluó de acuerdo a la transaminasa oxaláctica (Sgot). El tratamiento se consideraba beneficioso cuando la bilirrubina o SGOT bajaban un 50% a los 14 días del inicio de la terapia. De los 24 pacientes, 12 murieron, de los cuales 10 fueron debidos a insuficiencia hepática. El régimen hospitalario y el uso de los antibióticos eran ocasionalmente beneficiosos. En 32 de 37 casos ocurrieron recidivas que fueron suprimidas con el uso de la predmisona. De los 12 restantes casos que sobrevivieron 2 están en remisión sin esteroides, 10 en remisión con esteroides, de los cuales 4 están asintomáticos, 5 moderadamente sintomáticos y uno marcadamente afectado por la enfermedad. La 6-mercaptopurina determinó una remisión en 6 de los 7 casos en que fué utilizada, pero esta mejoría no podía mantenerse si se descontinuaba el farmaco. La disminución en los valores de SGOT no guardaba relación directa con las determinaciones concurrente de la bilirrubina sérica. En 6 casos en que existió la indicación se practicó la esplenectomía. Si algún beneficio ocurrió no pudo explicarse a base únicamente de la esplenectomía. De los 24 pacientes 3 estaban sufriendo de colitis ulcerativa. En 2 de ellos la colectomia e ileostomía no beneficiaron la condición hepática. Uno de los pacientes recibió mostaza nitrogenada y 2 de ellos fueron tratados con Cloroquina. En ninguno de los casos hubo alguna mejoría. El tratamiento de elección según los autores es el uso de los esteroides.

MIGUEL A. SARRIERA M.D.

**EFFECTS OF FREEZING ON THE GASTRIC MUCOSA OF DOGS** (Mecanismo de acción de la congelación gástrica sobre la mucosa de los perros). Tuvia Gilat, M.D., Paul Clapp, M.D., Julia Creemers, M.D., Manuel S. Tayao, M.D., Martin Lipkin, M.D., and Thomas P. Almy M.D. Andre and Bella Meyer Laboratory and the Departments of Medicine, Surgery and Pathology of Memorial Sloan-Kettering Cancer Center, The Second (Cornell) Medical Division of Bellevue Hospital, and the Department of Medicine, Cornell University Medical College, New York, N.Y. GASTROENTEROLOGY Vol. 46: 680-689 June 1964..

La reducción prolongada de la ácidez gástrica ha sido observada por algunos autores después de la congelación del estómago según la técnica ya descrita. Sin embargo otros trabajos han enfatizado el hecho de que a pesar

de esta hiposecreción gástrica, la mucosa de este, en especial sus células glandulares parietales y pepsinogenas no sufren cambios morfológicos significativos.

El artículo fué diseñado y realizado con el propósito de correlacionar las variaciones en la secreción ácida, morfología de la mucosa gástrica y la regeneración celular del epitelio gástrico.

La secreción gástrica fué determinada en dos ocasiones antes de la congelación y luego 1, 3, 6 y 8 semanas después de ésta. La biopsia de estómago se realizó por succión antes de la congelación y 24, 48, 96 horas y de 1 a 3 semanas después de la congelación. Las biopsias fueron estudiadas con el microscopio de luz y el electrónico. Se utilizó timidina H3 para la determinación de la regeneración epitelial.

Los resultados obtenidos por la congelación gástrica en los perros a temperaturas de -20 grados C de entrada y -12 grados C de salida a través de la gastrostomía practicada no demostraron ninguna reducción significativa en la secreción ácida bajo la estimulación con Histalog, insulina y peptona. Los estudios con el microscopio de luz y electrónico demostraban solo cambios transitorios y focales en las capas superficiales de la mucosa sin lesionar las células parietales y pepsinogenas. La regeneración del epitelio por mediación del uso de la Timidina H3 demostró que esta ocurría dentro de la primera semana a partir del primer día de la congelación. Después de 7 congelaciones de una hora de duración la mucosa gástrica y la secreción gástrica ácida eran normales. Se postula nuevos estudios para saber cual es el mecanismo fisiológico envuelto en los casos exitosos obtenidos con la congelación gástrica en pacientes con úlcera péptica.

MIGUEL A. SARRIERA M.D.

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**EFFECTS OF HYPERCAPNIA ON HISTAMINE STIMULATED GASTRIC ACID SECRETION** (Efecto de la hipercapnia sobre la acidez gástrica previo estimulo histamínico). A. Naitove, M.D., J. F. Penza, M.D. **GASTROENTEROLOGY**, 46:157, 1964.

Durante algún tiempo evidencia ha sido acumulado demostrando la Relación que existe entre los niveles sanguíneos de CO<sub>2</sub> y la secreción ácida gástrica. La inhalación de CO<sub>2</sub> o la hiperventilación, ha sido demostrado, aumentan la respuesta secretora gástrica en los perros sometidos a estimulación vagal, en el hombre sometido a una respuesta prandial y en la rata tanto a la respuesta prandial como a la estimulación con histamina.

Los autores estudiaron la acción de las variaciones del CO<sub>2</sub> en la secreción ácida gástrica previa estimulación con histamina según la técnica de De Vito y Harkins.

La hipercapnia inducida inhalando 75% de CO<sub>2</sub> en el aire durante 40 minutos produjo una disminución en la secreción de ácido gástrico. Variando la concentración de oxígeno no se obtuvieron cambios significativos en la secreción del ácido.

Los autores creen evidenciar el hecho de que las variaciones en el pH de la sangre puedan modificar la secreción gástrica durante la estimulación con el CO<sub>2</sub> aunque el artículo no justifica con hechos científicos tal pensamiento.

Estos resultados obtenidos usando histamina para estimular la secreción gástrica están en contradicción con los resultados previamente reportados utilizando la estimulación vagal en el perro y la respuesta posprandial en el hombre.

MIGUEL A. SARRIERA M.D.

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**MODIFICATIONS IN THE ELECTROCARDIOGRAM OF CEREBRO MENINGEAL DISEASES** (Les modifications d'électrogramme au cours des affections cérébro méningée). "ARCHIVES DES MALADIES DU COEUR ET DES VAISSEAX" - Paris - 56<sup>e</sup> Année No. 6 June 1963, Pages 650-664, Ives Bouurain, Raymond Houdart and Jean Paul Wiart.

The electrocardiogram of 87 patients presenting various cerebro-meningeal diseases and whose heart was presumed normal and where no anoxia or changes in blood pressure could be found have been studied. Special care was taken to relate this modification to the electrolyte and enzymatic picture. The most frequent modifications were: rhythm, rarely; bradycardia and auricular fibrillation and in the repolarization phase alterations such as T inversion and ST depression in standard leads as well as precordial leads and an U wave partially united to an ample T wave. These changes were followed by a series of electrocardiograms and a return to normality was seen in the subsequent tracings. These modifications were not related to any particular neuro localized lesion. The theories of myocardic anoxia and metabolic disturbances of potassium are presented and discussed. It is the belief of the authors based on animal experimentation and histologic studies that these modifications have their origin in a neurovegetative reflex; that the vegetative system has two ways of acting upon the myocardium: direct through the action of acetylcholine making easy the diffusion of potassium into the cells stabilizing in this way the potential of action of the membrane and adrenaline whose action is not known, but believed to diminish the permeability of potassium and increase the one of sodium and an indirect coronary action based in the sympathetic vasodilation and the parasympathetic vasoconstriction.

**FRANCISCO X. VERAY, M.D.**

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**THE PATTERN OF HEARING AFTER ACUTE OTITIS MEDIA** (Patrones auditivos subsiguientes a otitis media aguda). Olmsted, R. W., Alvarez, M.C., Moroney, J. D., and Eversden, M. J. Pediat. 65:252, 1964.

Se estudio el patrón auditivo por medio de pruebas audiometrías en 82 niños desde 2  $\frac{1}{2}$  hasta 12 años de edad, que habían sufrido otitis media aguda. Los estudios se hicieron aproximadamente a la semana, un mes, dos, tres y seis meses después del ataque de otitis. La interpretación de disminución auditiva fue a base de requisitos de intensidades de 15 dbs. o más para percibir el sonido.

Se dividieron los niños en cuatro grupos a base de los resultados. En el grupo I, de 27 niños, o sea el 33% no hubo disminución auditiva. En el grupo II hubo disminución auditiva que desapareció durante el período de seis meses de observación. En este grupo habían 33 niños, o sea el 40.2%. En el grupo III hubo una disminución auditiva inicialmente que persistió durante los seis meses de observación. En este grupo había 10 niños, o sea el 12.2%. Se aspiró líquido seroso del oído medio en tres de estos pacientes, pero no hubo mejoría dramática en la audición después del procedimiento. En la categoría IV se observó disminución auditiva inicialmente que persistió de 1 a 4 meses pero no había observación ulterior de estos pacientes. En este grupo había 12 niños, o sea 14.6%.

El estudio demuestra que un número importante de niños tienen disminución auditiva por un período de tiempo variable después de una otitis media aguda.

**J. E. SIFONTES, M.D.**

**MAMMOGRAPHY (Mamografía). P. Strax, Current Medical Digest 30:39 (Dec.) 1963.**

Many investigators believe that, with currently available treatment methods, the only way to increase survival rates in breast cancer is earlier detection and treatment. Mammography may provide a means for detection of these neoplasms before they can be found by inspection and palpation. Mammography is also valuable in differential diagnosis; provides an opportunity for study of the processes which occur in the breast with, possibly, in the future, a way to identify early cancerous changes; affords information as to changes which can be correlated with the endocrine status of the individual; helps to convince the patient of a need for treatment or allays the fears of an over-anxious patient.

Basic principles were developed by Leborgne in the early 1950's. In the United States, the most commonly used techniques are those developed by Gershon-Cohen and Egan. To obtain a good mammogram, the film must include all of the breast and must be sufficiently dense so that small calcifications can be seen. Patients must be positioned so that motion, with consequent blurring, is avoided and so that accurate location of the lesion as to quadrant is possible. Experience is necessary in interpretation, and a minimum study of 500 cases is necessary before the radiologist can achieve much success. Distinguishing the normal breast patterns is the most difficult problem, because changes associated with cancer are also found in the normal breast. Early cancer may appear small and innocuous and identification of a cancerous change must be made from the degree and association of several variations. Cancer is diagnosed by such direct signs as dominant mass and microcalcifications and such indirect signs as thickened skin, nipple deformity, enlarged veins, and altered architecture.

**ISIDRO MARTINEZ, M.D.**

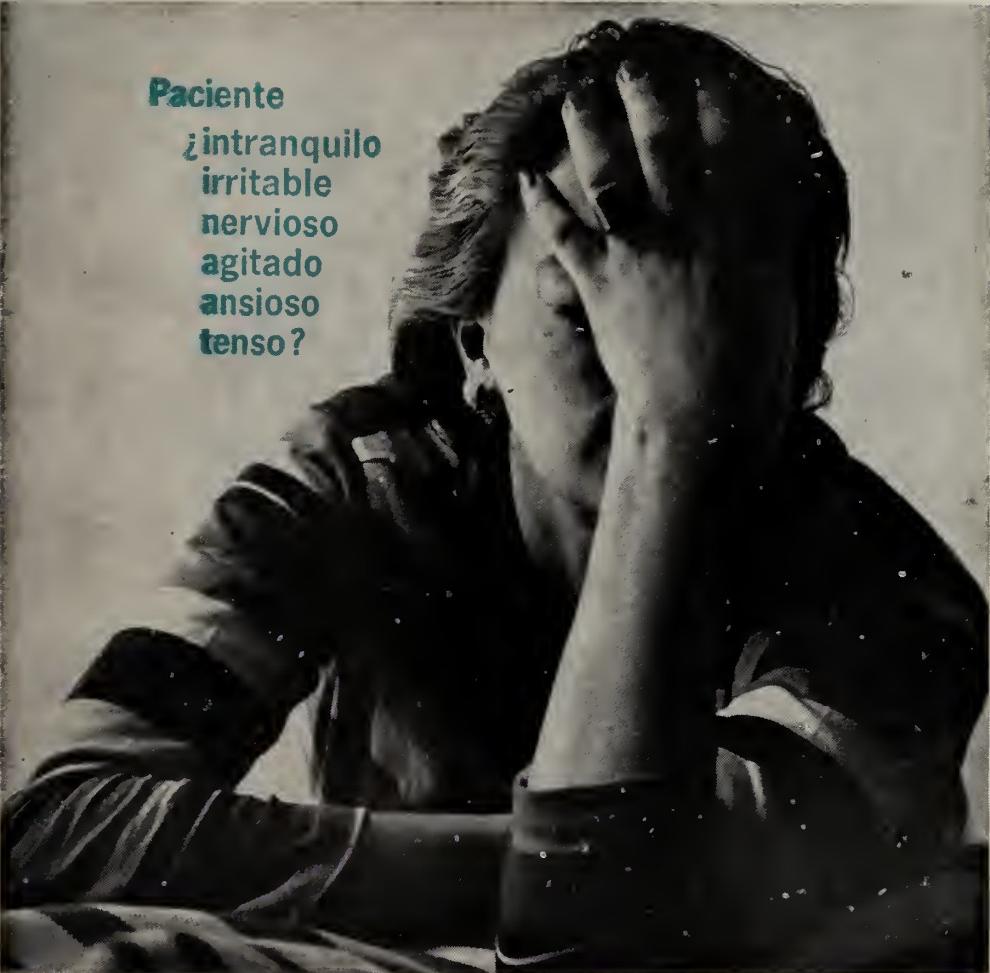
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## SECTION 1 (continued)

### 4. Free Choice of Physician

(a) The Judicial Council calls attention to the third point of the Ten Principles adopted in Cleveland in 1934 which defines "free choice of physician." This the Council interprets to mean not only the patient's right to choose any physician desired but also, conversely, the physician's right to accept or reject any patient requesting his services under the plan. It also expressly requires that any qualified, licensed physician residing in the area in which the plan operates be allowed to participate. Thus we see that to be a participating doctor in a voluntary plan it is not necessary for one to be a member of the American Medical Association. It is, however, necessary for him to accept and obey the terms of the contract offered by the plan, and on violation of the terms he may be dropped from the rolls, if the violation seems sufficiently grave for such action. It is needless for us to remind members that any violation of this provision would indeed deprive the public of the choice of a great many physicians. As the voluntary plans are intended to cover and supply sufficient medical care of high quality for the whole country, with no feature of a compulsory system, it is necessary that the principle be strictly observed. However, it is tacitly understood that any contract between an approved voluntary medical plan and a doctor includes an understanding that the ethics of the American Medical Association will not be violated. These basic points also require that the medical profession determine the adequacy and character of the hospitals. All hospitals approved by the local physicians and willing to accept the terms of the plan should be allowed to participate. In order that a high standard of medical service be maintained, hospitals may limit somewhat the number of physicians who deliver medical service in their institutions and even assign a physician to certain definite fields in accordance with his training and experience. The widest possible use of hospitals approved by the local profession should be encouraged in order not to limit the number of doctors made available for the plan. Under no circumstances shall doctors working under this plan be forced to send patients to a particular hospital unless it is the only one approved in that area. (1947 Report)

(b) The phrase "free choice" of physician is more and more frequently used and there is a general understanding of what the phrase means. Actually no person can have an absolutely free choice for many reasons, and if his freedom of choice is not absolute then it is not free but limited. Chapter II, Section 3 of the Principles (1955 edition) states: "A physician is free to choose whom he will serve." Therefore the physician whom the patient chooses may decline to serve when he is chosen, or the chosen physician may be unavailable for many reasons. (House of Delegates, 1937)



**Paciente**

**¿intranquilo  
irritable  
nervioso  
agitado  
ansioso  
tenso?**

**Cuando la tensión nerviosa  
se torna insopportable, recete**

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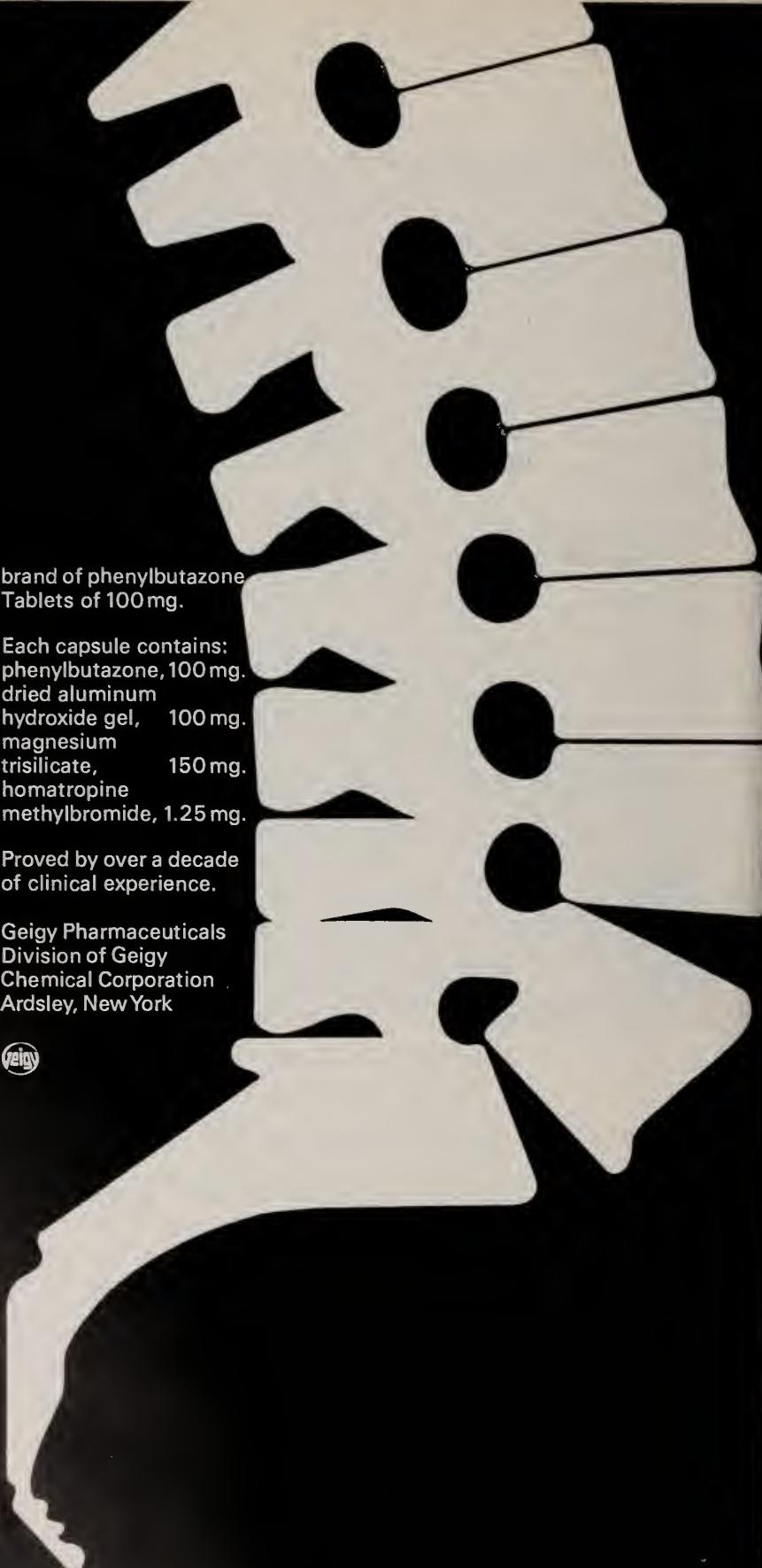
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by Dr. F. Maria Segovia de Arana

"Thus, olive oil is unique among vegetable oils by reason of its organoleptic characteristics. Its natural aroma and taste are regarded pleasant by the consuming public in all countries. It need not be refined: it is the only oil that can be consumed in the West in its natural state. This is most important, because in the course of refinement, oils are to some extent transformed and lose some of their nutritive properties."

### COMPOSITION AND CHEMICAL PROPERTIES OF OLIVE OIL

"In the chart below, taken from Hilditch (The chemical constitution of natural fats) the composition in saturated fatty acids (miristic, palmitic and stearic and non saturated (oleic and linoleic) of olive oil in various countries is shown.

#### OILS.

	Miristic	Palmitic	Stearic	Oleic	Linoleic
Italy (Tuscany)	1,1	9,7	1,0	79,8	7,5
Córcica	1,1	9,4	2,0	84,5	4,0
California	1,1	7,0	2,3	85,8	4,7
Spain	0,2	9,7	1,4	81,6	7,0
Tunis	1,1	14,7	2,4	70,3	12,2
Palestine	0,5	10,0	3,3	77,5	8,9
Greece (Rhodes)	0,4	19,7	0,3	69,6	10,4

As can be seen, olive oil, apart from containing a large proportion of a non saturated fatty acid, of twofold linkage, namely oleic acid, also contains lesser quantities of others that have more than a twofold linkage."

## PHITOSTERINES

"Olive oil contain "phitosterine", which, as its name indicates consists of vegetable sterines similar to the colesterine of animal fats, but with the interesting biological characteristic that they are not absorbed by the wall of the stomach and what is even more important, that they prevent, to a greater or lesser extent, the intestinal absorption of the colesterine contained in food, as has been recently demonstrated by the experiments carried out by the Chaikoff School in the United States."

## ARTERIOSCLEROSIS AND OLIVE OIL

"The experiments carried out by Dr. Bronte Stewart in South Africa, demonstrated that cholesterol in the blood increased when the subjects consumed animal fats, but this did not occur with vegetable fats, such as sunflower oil, olive oil, etc.

The same type of result was achieved by a group of investigators (among others, Dr. P. D. White, President Eisenhower's personal physician, and Dr. Keys) in a test carried out in Calabria and Crete on subjects whose ages varied between 45 and 65 years and the fatty part of whose food consisted almost entirely of oil. Only two out of the 657 persons examined were seen to have had heart attacks. When this group was compared with a similar one, as regards age, in the United States, whose diet largely included large quantities of animal fats, sixty cases of heart attacks were discovered.

("Time" magazine, 30 December 1957)."

## CONCLUSIONS OF THE WORK OF DR. SEGOVIA DE ARANA

"We must be careful and only recommend such things as can reasonably be expected to do more good than harm. In our opinion, the following measures are reasonable and well founded:

- 1) Reduce the total consumption of calories and in particular those derived from fats, to the amounts consumed, (and which quantities should be maintained) when the body weight is normal between twenty one and twenty five years of age. It is advisable to use non saturated vegetable oils in lieu of animal fats.
- 2) Take active daily physical exercise.
- 3) Avoid all excess (tobacco, alcohol, emotional tension) but such habits need not be cut down drastically.
- 4) Treat arterial hypertension if it appears."

"Through the courtesy of Torres & Ribelles, S. A., Seville, Spain, proprietors of the famous Spanish Olive Oil brand **BETIS**



# Terramicina\*

MARCA DE LA OXITETRACICLINA

## GOTAS PEDIATRICAS premezcladas

en fórmula especial para niños

y su aliado

## JARABE premezclado

preferida universalmente por los enfermos  
pediátricos y geriátricos

Ambos preparados tienen un atractivo sabor  
a cereza silvestre

No hay rebeldías en el momento de tomar  
la medicina

Ambos están listos para ser administrados  
sin reconstitución. No se pierde tiempo  
en su preparación

Ambos son estables durante dos años a la  
temperatura ambiente, aun después de abrir  
el frasco. Se conserva la alta potencia y la  
dosificación es siempre exacta

Ambos contienen Terramicina, el antibiótico  
de amplio espectro antibacteriano más  
ensayado y mejor comprobado, en la forma  
que mejor sabor tiene

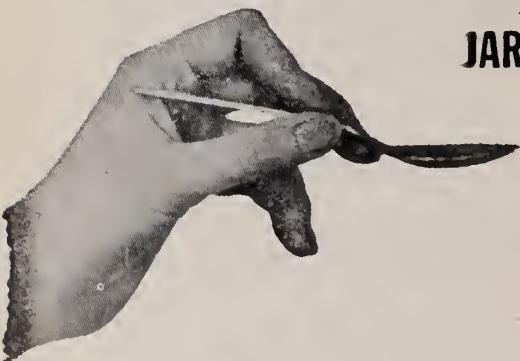
GOTAS, con 100 mg. por cc., en frascos-ampollas  
de 10cc. con cuentagotas calibrado a  
25 mg. y 50 mg.

JARABE, en frascos de 60 cc., con 125 mg.  
por cucharadita de 5 cc.



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PREPARADOS VITAMINICO-MINERALES - HORMONAS



TERRAMICINA



PIEDRA ANGULAR  
DE LA CLINICA



## For the anxious patient under stress

# Mellaril®(thioridazine) reduces "the emotional cost of living"

The business of living engages us all in a continuity of stress situations. It is only when the patient constantly overreacts to these situations—at excessive emotional cost—that clinical "anxiety" may occur. Health problems, financial pressures, household difficulties, the frustrations of old age—these are among the daily sources from which the anxiety and tension are generated, often in moderate to severe proportions.

Mellaril (thioridazine) relieves such anxiety, helping the patient to deal competently with the stresses of everyday life. Non-habituating, it can be given for extended periods of time. It does not "separate" the patient from practical problems and pressures, does not induce euphoria or a fuzziness which can compromise the ability to cope with realities. Rather, it helps the patient move more competently in his daily world by eliminating useless tension, by allowing him to conserve emotional resources and energies, and to direct them against the problems really worth worrying about. When efficacy is thus combined with a remarkable minimum of side effects, the physician is indeed

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*For moderate to severe anxiety, the recommended initial dosage is 25 mg. t.i.d.*

*Indications: Anxiety, tension and agitation in pediatric, adult, and geriatric patients. Psychomotor hyperactivity in psychotic patients.*

*Side Effects:* Jaundice has not been observed. Occasional drowsiness, dryness of the mouth, nasal stuffiness, skin eruption, nocturnal confusion, galactorrhea, amenorrhea, orthostatic hypotension, inability to ejaculate in the male, pseudoparkinsonism. Pigmentary retinopathy has been reported in doses in excess of 1600 mg. daily given over long periods of time. Leukopenia, agranulocytosis, photosensitization, and convulsive seizures are extremely rare, but are possible complications of all phenothiazine administration.

*Contraindications: Any severely depressed or comatose state.*

"In cases of hemorrhage from the nasal cavity, regardless of the bleeding site . . . the use of this drug [ADRENOSEM] virtually obviates the use of anterior or posterior nasal packing or cautery in any form."<sup>1</sup>



Peele<sup>1</sup> like others<sup>2,3</sup> has found that Adrenosem safely and effectively checks oozing bleeding in conditions such as epistaxis because Adrenosem maintains the integrity of capillaries.

Adrenosem is effective in epistaxis because it maintains capillary integrity by decreasing capillary permeability and promoting retraction of severed capillary ends. Unlike coagulants, Adrenosem does not mediate its action through the clotting mechanism which is often found to be normal in spite of active bleeding.

Adrenosem is indicated and proved safe for use wherever integrity of small blood vessels is impaired such as threatened abortion, capillary hemorrhage during anticoagulant or X-ray therapy, ecchymosis, purpas, ulcerative colitis and certain types of metrorrhagia and menorrhagia.

*Consult package insert or PDR, pages 739-741 for more detailed information.*

# adrenosem®

SALICYLATE •

(brand of carbazochrome salicylate)

\*U.S. Pat. Nos. 2581850; 2506294

**Safety:** There are no contraindications to Adrenosem at recommended dosages.

**Dosage and Administration:** In epistaxis and other nonsurgical uses: In presence of active bleeding, 1 or 2 cc. (5 to 10 mg.) I. M. followed by maintenance dosage of 1 to 10 mg. (avg. 2.5 mg.) t.i.d. orally.

**Supplied:**

*For I.M. Injection Only*—Ampuls, 5 mg./cc., pkgs. of 5 and 100; 10 mg./2 cc., pkgs. of 5.

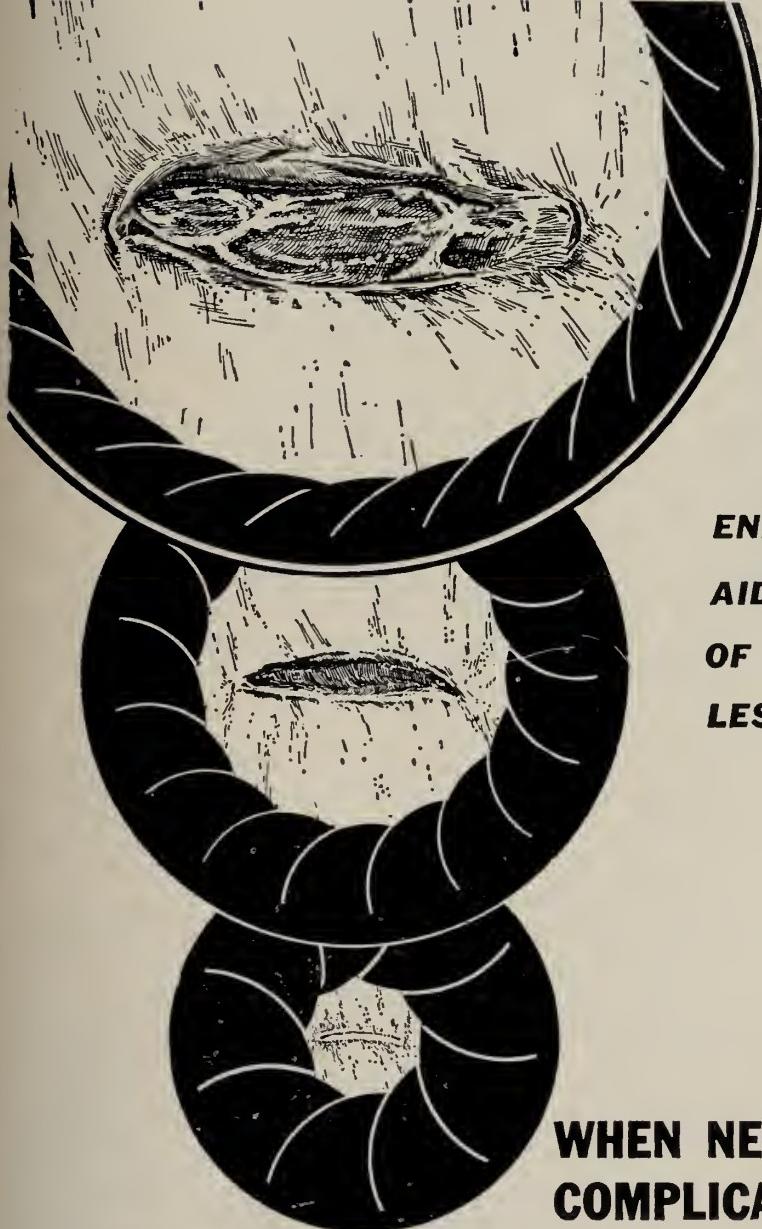
*For Oral Administration Only*—Tablets, 1 mg. (s.c. orange), 2.5 mg. (s.c. yellow), bottles of 50.. Syrup, 2.5 mg./5 cc. (1 tsp.), bottles of 4 oz.

**References:** 1. Peele, J. C.: Med. Times 86:1228 (Oct.) 1958; 2. Riddle, A. C., Jr.: Oral Surg., Oral Med., Oral Pathol. 8:617 (June) 1955. 3. Lamphier, T. A.: Clin. Med. (Dec.) 1962.

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**PARKE-DAVIS**

**ENZYMATICALLY  
AIDS HEALING  
OF EXUDATIVE  
LESIONS ...**

**WHEN NECROTIC TISSUE  
COMPLICATES HEALING**

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EJ-12-63



not all but *Most*  
bacterial respiratory  
tract infections  
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therapeutically  
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erythromycin



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**Usual Adult Dosage:** 250 mg. every six hours.

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ANTIBIOTIC GIVE UP  
TO 2 EXTRA DAYS'  
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Because it is more resistant to disintegration, has a lower renal clearance rate than earlier tetracyclines'... a favorable depot effect resulting from protein binding and greater mg. potency... all giving higher, sustained *in vivo* activity which continues long after the last dose.

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**Effective** in a wide range of everyday infections — respiratory, urinary tract and others — in the young and aged — the acutely or chronically ill — when the offending organisms are tetracycline-sensitive.

**Side Effects** typical of tetracyclines which may occur: glossitis, stomatitis, proctitis, nausea, diarrhea, vaginitis, dermatitis, overgrowth of nonsusceptible organisms. Also: photodynamic reaction (making avoidance of direct sunlight advisable) and, very rarely, anaphylactoid reaction. Reduce dosage in impaired renal function. The possibility of tooth discoloration during development should be considered in administering any tetracycline in the last trimester of pregnancy, in the neonatal period, and in early childhood. Capsules, 150 mg. and 75 mg. of demethylchlortetracycline HCl. Average Adult Daily Dosage: 150 mg. q.i.d. or 300 mg. b.i.d. 1. Kunin, C. M.; Dornbush, A. C., and Finland, M.: Distribution and Excretion of Four Tetracycline Analogues in Normal Young Men. *J. Clin. Invest.* 38:1950 (Nov.) 1959.

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c) Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: (1) introducción, (2) material y métodos, (3) resultados, (4) discusión, (5) resumen (en español e inglés), (6) referencias.

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g) Deben usarse los nombres genéricos de los medicamentos. Pueden usarse también los nombres comerciales, entre paréntesis, si así se desea.

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i) Las fotografías y microfotografías se someterán como copias en papel de lustre sin montar. Los dibujos y gráficas deben prepararse a tinta negra y en papel blanco. Todas las ilustraciones deben estar numeradas (números árabigos) e indicar la parte superior de las mismas. Debe escribirse una leyenda para cada ilustración e indicarse en el texto donde debe ir colocada. Un máximo de 6 ilustraciones, por artículo, serán permitidas sin costo para el autor.

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a) The entire manuscript, including figure legends and references, should be typewritten double-spaced in duplicate with ample margins.

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d) Case reports will include (1) introduction, (2) description of the case, (3) discussion, (4) summary in English and Spanish and (5) references.

e) Tables, footnotes and legends to figures should appear in separate sheets.

f) If paper has been presented at a meeting the place and date of this should be stated.

g) Generic names of drugs should be used. Trade names may also be given in parenthesis if desired.

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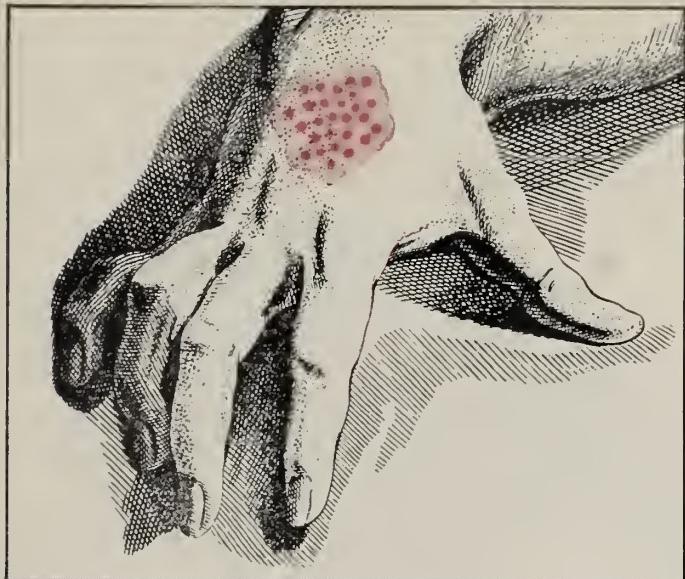
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to eradicate signs and symptoms of  
allergic or inflammatory dermatoses

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(betamethasone<sup>0.6 mg.</sup>  
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**Dosage and Administration:** The dosage of Celestone (betamethasone) must be adjusted to individual patient requirements; i.e., severity of the condition, anticipated duration of therapy, tolerance to the steroid and response obtained. The lowest effective dose should be employed. When corticosteroid therapy is no longer required, the dosage of this drug should be reduced gradually and then discontinued. Withdrawal of therapy should be gradual. Package literature should be consulted for detailed dosage schedules.

**Precautions:** Although Celestone (betamethasone) differs significantly in potency and electrolyte effects, it is a corticosteroid and hence is potentially capable of causing any of the reported side effects of other such compounds. As with other corticosteroids, recurrence

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For complete product details, consult Schering literature available from your Schering representative, or Medical Services Department, Schering Corporation, Union, New Jersey.

**Packaging:** Bottles of 30, 100, 1000. Tablets of 0.6 mg. each. \*TRADEMARK CC-SAS-J-PR

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10 mg.,
5 mg.
12 mg.
0.2 mg.
q.s.
5%
100 mg.

**Dosage:** Adults, 1 teaspoonful every two or three hours. Children, six to twelve years:  $\frac{1}{2}$  teaspoonful every two or three hours. Do not exceed 7 doses daily. Administer to children under six years of age only on the direction of a physician, and do not exceed the recommended dosage.

**Supplied:** Conar—2 oz. bottles, Pints, Gallons; Conar Expectorant—Pints, Gallons.

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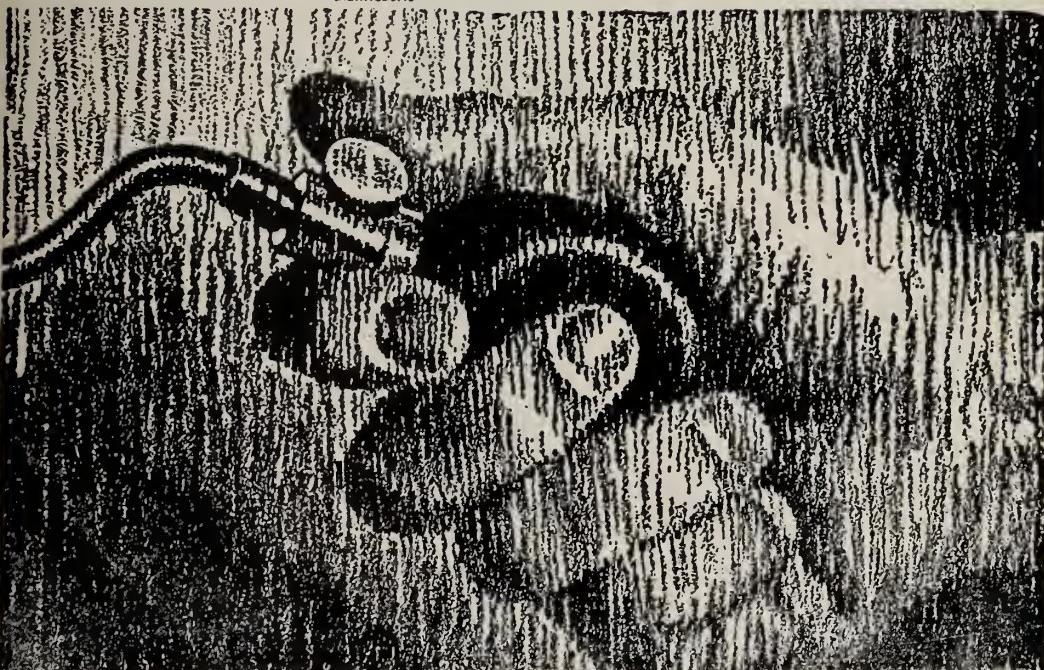
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Versatile in indications—recommended in sustained essential hypertension, and in those labile forms unresponsive to sedative therapy.

Effective "around-the-clock"—continuously and significantly reduces lying, sitting and standing pressure; simple dosage adjustment can prevent morning hypotension without sacrifice of afternoon control.

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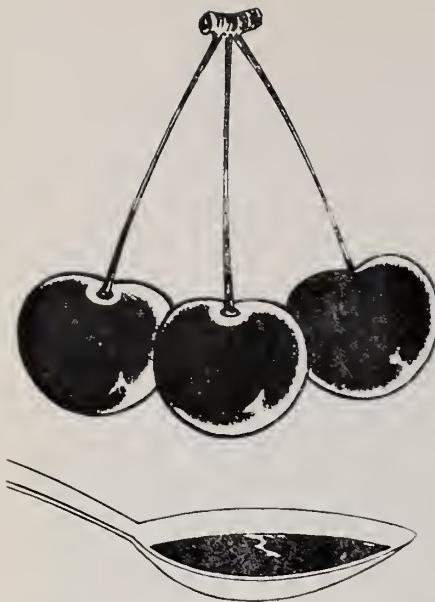
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**Precautions:** Side effects are rare. If a patient should show signs of sensitivity, countermeasures (e. g., epinephrine, steroids, etc.) should be administered or the drug withdrawn. Erythrocin does not materially alter the normal intestinal flora and only very rarely has resulted in intestinal overgrowth of pathogenic bacteria, yeasts, or molds. Nevertheless, this possibility should be kept in mind.

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1. Cirelli, M.G., Del. St. Med. J., Vol. 34, Núm. 6, Pág. 159, junio, 1962



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en fórmula especial para niños

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## JARABE premezclado

preferida universalmente por los enfermos  
pediátricos y geriátricos

Ambos preparados tienen un atractivo sabor  
a cereza silvestre

No hay rebeldías en el momento de tomar  
la medicina

Ambos están listos para ser administrados  
sin reconstitución. No se pierde tiempo  
en su preparación

Ambos son estables durante dos años a la  
temperatura ambiente, aun después de abrir  
el frasco. Se conserva la alta potencia y la  
dosificación es siempre exacta

Ambos contienen Terramicina, el antibiótico  
de amplio espectro antibacteriano más  
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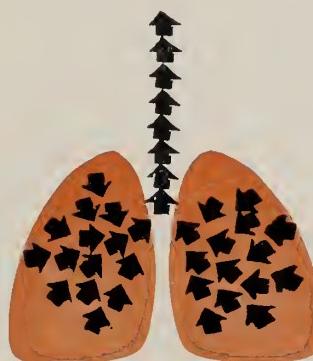
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**Side Effects:** Skin rash, GI disturbances, weakness or dizziness may occur, usually controllable by reducing dosage or correcting electrolyte imbalance. Pre-existing electrolyte abnormalities may be aggravated. Possibility of potassium depletion is greater in cirrhotics and digitalized patients. Foods rich in potassium may be desirable. Possibility of azotemia is greater in renal disease; and of hyperglycemia and glycosuria in diabetes. Photoallergy and hyperuricemia predisposing to gout have occurred. There may be a sudden drop in blood pressure when given with ganglionic blocking agents, veratrum or hydralazine, requiring reduction in dosage of these other drugs.

**Precautions:** Anuria.

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# BOLETIN

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## EVALUACION CLINICA DE PRUEBAS DIAGNOSTICAS EN LA FUNCION TIROIDEA CON I-131

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HADDOCK, M.D.,\*\*\* y MANUEL E. PANIAGUA, M.D.\*\*\*\*

De todas las pruebas que con radioisótopos se han intentado para medir la función tiroidea, una de las primeras, y con mucho, la más conocida y utilizada por los médicos en la rutina diaria, es la captación de yodo (I-131) a las 24 ó 48 horas. Esto nos da la medida de la avidez de la glándula por incorporar yodo, que es una de las etapas en el metabolismo de este elemento, y, en la gran mayoría de los casos, está en relación directa con la actividad general de la tiroides. Siempre se debe recordar, que, en algunas circunstancias, dicho metabolismo está alterado en etapas posteriores y la captación entonces puede no reflejar el estado clínico del paciente, debiéndose en estos casos recurrir a pruebas especiales para complementar el estudio y llegar al diagnóstico correcto. Conociéndose esas limitaciones y dándole la interpretación que le corresponde por sí sola o junto con dichas pruebas complementarias, la captación de I-131 constituye un muy valioso elemento diagnóstico para las disfunciones tiroideas.

En ésta, como en la mayoría de las pruebas de laboratorio, que se realizan en medicina, pequeñas variaciones en la técnica pueden reflejarse en los resultados. En la misma forma las variables que actúan sobre el grupo de pacientes con los cuales se debe trabajar en cada centro, pueden incidir en los valores que deberán ser considerados como normales y por fuera de los cuales se puede diagnosticar una alteración de la función. Ello hace que fijada una técnica en todos sus detalles y conociendo el tipo de población con la cual se va a trabajar, se deba hacer un estudio estadístico de los resultados obtenidos en un número significativo de pacientes, para establecer los límites que se aceptarán para individuos normales o patológicos. Esto con toda la elasticidad que los procesos biológicos exigen. Prueba de ésto son los diferentes

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valores que han comunicado los distintos autores según los equipos disponibles, la técnica empleada y sobre todo el tipo de población que forma la mayoría de los pacientes a estudiar en cada servicio. Se ha considerado de interés, de acuerdo con ésto, realizar con los valores de la captación de I-131 a las 24 horas medidos en el Centro Nuclear un estudio estadístico y de él deducir los valores eutiroideos para la población hospitalaria referida a este Centro y el margen de seguridad diagnóstica de esos valores.

### Material

Se ha realizado el análisis de algo más de 800 historias clínicas de pacientes pertenecientes a los Hospitales Universitario y Municipal de Río Piedras que han sido enviados al Centro Nuclear para determinación de su actividad tiroidea mediante la captación de I-131 a las 24 horas. De estas historias se han seleccionado 263 pacientes cuyos cuadros clínicos pudieron considerarse bien definidos: 93 como eutiroideos, 84 hipertiroideos; 24 hipotiroideos y 62 bocios no tóxicos. En todos los casos el cuadro clínico determinó la selección de los grupos estudiados. Debido a que el material seleccionado procede de individuos que han sido referidos para estudiarse sospechando enfermedad no se usará el término normal para ningún valor de la prueba cuyo cuadro clínico sea clara y definitivamente eutiroideo. A ese criterio clínico se agregó en 173 casos un resultado concordante en el dosaje de colesterol plasmático y en 42 el metabolismo basal y dosaje de yodo proteíco sérico. De todos ellos el 13% era del sexo masculino y el resto femenino, proporción que se observa en general en la frecuencia de las alteraciones tiroideas. La edad oscilaba entre 6 y 87 años. Se interrogó a los pacientes para descartar la influencia de yodo exógeno o cualquier otro elemento que pudiera variar los valores de captación o de algún tipo de enfermedad no glandular de las que pueden influenciar en la actividad tiroidea. Las mediciones se efectuaron con tubo de centelleo con cristal de INa activado con Ta de 2" x 2" con colimación de diámetro sobre el cristal a 3 pulgadas de la superficie de 2" y en la salida de 3-1/2" con un filtro de plomo de 1/16" (filtro A de Brucer)<sup>1</sup> conectado a un estalímetro decimal.

### Método

Se administró a los pacientes por vía oral una dosis diagnóstica que varió entre 5 - 100 uc. Esta variación estuvo condicionada a la edad del paciente o a que éste tuviera que hacerse simultáneamente otra prueba como es yodo proteíco (I-131) relación de conversión o nivel plasmático o gamagrama. No se consideró importante que estos hubieran o no desayunado ya que la medición

iba a efectuarse a las 24 horas. A las 24 horas se realiza la medición de la actividad y el cálculo de la captación dos veces en cada paciente para control y haciendo en cada medición un conteo no menor de 10,000 cuentas.

La posición del paciente con respecto al tubo y la medición del fondo ha variado tres veces en nuestro laboratorio debido a razones de comodidad y a los elementos de que se ha ido disponiendo. Esas posiciones han sido:

a) La actual—Paciente acostado — Cuello medido a 20 cm con filtro A de Brucer y testigo en un fantoche de lucite de dispersión semejante al tejido vivo, en igual condición, el fondo en uno y otro se midió manteniendo el tubo en la misma posición e intercalando un filtro de plomo de 4 x 4 pulgadas y media pulgada de espesor (filtro B de Brucer) lo más cerca posible del objeto a medir (Técnica de Brucer).

b) Paciente sentado — todo el resto en las mismas condiciones que en la anterior, y

c) Paciente sentado — medición de cuello y fantoche igual—“back-ground” para cuello se consideraba la actividad del tercio inferior del muslo y para el testigo, directamente la actividad del aire.

Para verificar si era correcto incluir en este estudio a todos los pacientes seleccionados, pese a haber sido medidos en tan distintas condiciones geométricas, se tomó un grupo de 26 individuos y se les midió sucesivamente en las tres posiciones, con la misma dosis y manteniendo fijas todas las otras variables. El resumen de los resultados obtenidos son los que figuran en el cuadro No. 1. Las variaciones son tan pequeñas que no ameritan análisis estadístico para determinar su significación, ya que por el examen superficial se puede apreciar que las diferencias de las medidas del paciente en cualquiera de las tres posiciones son insignificantes. De cualquier manera se hizo el análisis estadístico de desviación (Método de Friedman en Siegel)<sup>2</sup> el cual confirmó lo antes dicho.

CUADRO I

	Pos. A.	Pos. B.	Pos. C.
Promedio	26.8	26.2	26.1
Desviación			
Típica (Std.)	17.4	16.7	16.2
Rango (range)	8.8 - 72.1 (63.3)	8.6 - 71.6 (63.0)	8.7 - 69.8 (61.1)

Los cálculos realizados son los comunes para determinación del porcentaje.

$$\% \text{ captación} = (\text{Med. cuello} - \text{fondo cuello}) \times 100$$

---


$$\text{Med. tes.} - \text{Fondo test.}$$

## Resultados

Los resultados obtenidos en los 263 pacientes han sido estudiados estadísticamente habiéndose llegado a las conclusiones que aparecen en el cuadro No. 2.

CUADRO NO. 2

Diagnóstico	No. Pac.	Med. Arit.	Desv. Std.	Error Estadist.	Mediana	Rango
Eutiroideo	93	25.3	± 8.4	± 1.7	23.5	13.2 — 67
Hipertiroideo	84	69.1	± 13.9	± 1.5	70.5	31.6 — 97
Hipotiroideo	24	6.1	± 5.7	± 1.2	3.9	1.1 — 20.7
Bocio simple	62	27.3	± 12.9	± 1.6	21.3	7.7 — 81.9

## Discusión

Puede considerarse al grupo estudiado como proveniente de gran parte de la población de la Isla, ya que, si bien el Hospital de Río Piedras presta atención esencialmente a pacientes que viven en ese distrito, el Hospital Universitario en cambio recibe sus casos de todos los centros asistenciales del noreste del país. La amplitud del rango de edades de 6 a 87 años, siendo los más numerosos de 20 a 40 y la proporción entre los distintos sexos es la que suele verse en la frecuencia de las afecciones tiroideas. La población examinada no era muy numerosa para subdividirse en grupos suficientemente grandes para obtener datos válidos sobre si pudieran haber diferencia por sexo y edad. Sin embargo se recogió la

EUTIROIDEO

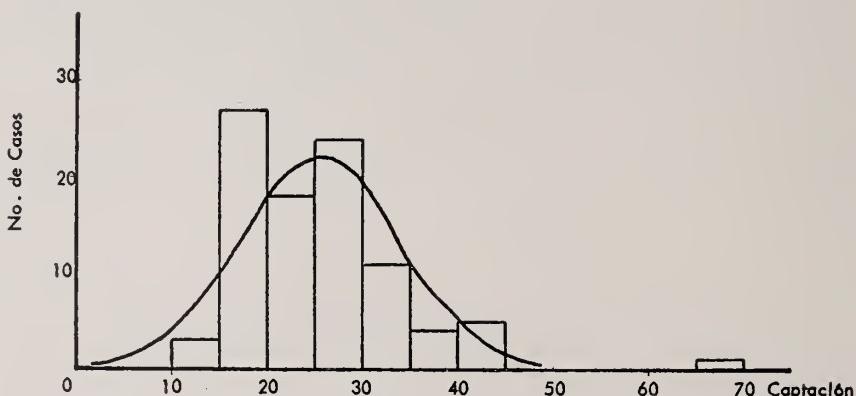


GRAFICO 1

## HIPERTIROIDEOS

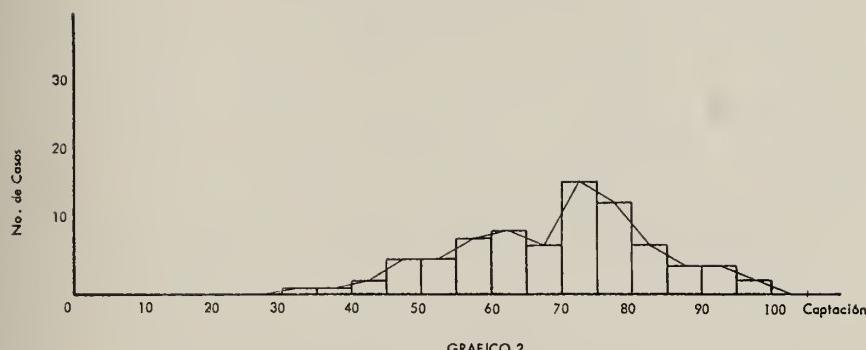


GRAFICO 2

impresión de que estos dos factores no afectaban la prueba excepto en niños que parecía ligeramente superior que en el resto de la población.

La proximidad de media y mediana en los estudios estadísticos indica una distribución uniforme de las series especialmente en eutiroideos e hipertiroideos, no lo son tanto los hipotiroideos y boscios no tóxicos, pero los primeros constituyen el grupo menos numeroso y en los segundos es de esperar una mayor y más irregular dispersión de los valores por la variación de las condiciones geométricas debidas especialmente al distinto tamaño de la glándula (gráficos 1, 2, 3, 4). La superposición entre eutiroideos e hipertiroideos da una inseguridad en los diagnósticos para nuestros casos de sólo el 5% en cada grupo que está por debajo de la inseguridad que citan Beierwalters,<sup>3</sup> Silver,<sup>4</sup> Quimby,<sup>5</sup> Johns y colaboradores<sup>6</sup> y otros. Esa superposición es mucho mayor para los hipotiroideos comparados con los eutiroideos posiblemente debido a que en nuestro medio los valores inferiores de captación en pacien-

## HIPOTIROIDEOS

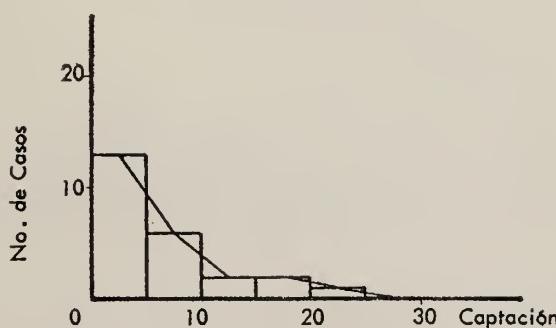


GRAFICO 3

## BOCIO SIMPLE

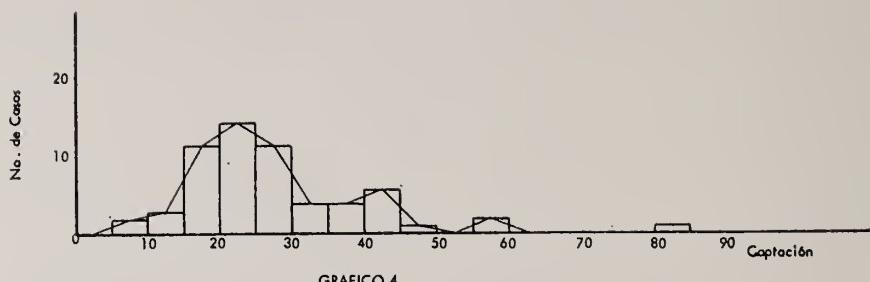


GRAFICO 4

tes eutiroideos son, en general, más bajos que los comunicados por otros autores (gráfico 5). Johns y col.,<sup>6</sup> Lanaro y López Verde,<sup>7</sup> Soto y col.,<sup>8</sup> Stanbury y col.,<sup>9</sup> Rúa y col.,<sup>10</sup> etc. La observación de la distribución de los valores eutiroideos nos muestra, además, de un promedio bajo en relación a los obtenidos en otros países, de acuerdo a los trabajos recientemente citados, una gran concentración de resultados entre 15 y 30%. En Puerto Rico tenemos valores comunicados por el Dr. Busó<sup>11</sup> que concuerdan con los nuestros, de 15 a 45%, en pacientes eutiroideos en general, mayores de 50 en hipertiroideos y entre 0 y 10 para hipotiroideos, con mayor superposición entre eutiroideos e hipofuncionantes.

Entre las causas a las que podría atribuirse esos valores relativamente bajos, debemos tener en cuenta fundamentalmente:

- 1) La proximidad del mar a todas las zonas estudiadas la que aumenta la proporción de yodo del aire, agua, vegetales, etc.
- 2) El tipo de alimentación que incluye mariscos, pescado, especialmente bacalao que contiene también mucho yodo.

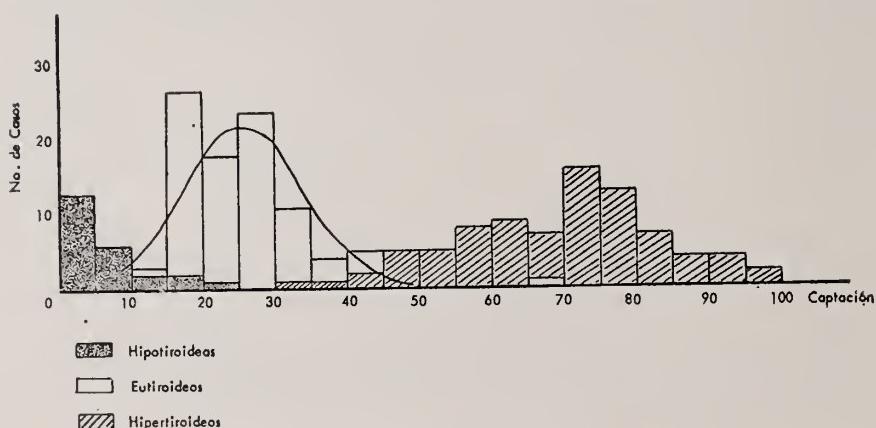


GRAFICO 5

### 3) El consumo de sal yodada por la población.

Otras fuentes de yodo en nuestro medio, son ya comunes en todos los países como ser polivitamínicos tomados indiscriminadamente, y otras drogas que deprimen la captación por lo que no serían causa tan probable de estos resultados.

Las tres razones enunciadas mostrarían que ese promedio bajo de captación no corresponde a déficit de función glandular sino a cierto grado de saturación yodada de la glándula. En Chile con igual cercanía al mar Barzelatto y col.<sup>12</sup> hallan una medida aritmética de 20% y en Filipinas sin embargo Campos, P. C. y col.<sup>13</sup> dan media de 31.5 pero con desvío de  $\pm 11.4$  y en apoyo además de esas razones podemos decir que en Mendoza, Argentina en zona boccosa, en 1951 Stambury y col.<sup>9</sup> hallaron una media de 58.5% y después de la administración de sal yodada a esa misma población durante 6 años, Perinetti y col.<sup>14</sup> publican un nuevo cálculo estadístico que da un promedio de captación de 29.8%.

### Conclusiones

Los resultados obtenidos en este estudio nos permiten aceptar los valores de 8 a 45% de captación tiroidea de 24 horas como los valores de función eutiroidea en pacientes de nuestro medio y de acuerdo con la técnica que se usa en el Centro Nuclear ( $25.3 \pm 2$  desviaciones standard de 8.4 con un error diagnóstico de 5%). Debido a la mayor superposición el error diagnóstico entre eutiroideos e hipotiroideos es también mayor: para los primeros es de 8% y para los últimos es de 30%.

Los valores obtenidos por encima o por debajo de esos límites (8 y 45%) podrán ser considerados hiper o hipotiroideos respectivamente, siempre con ese margen de error. Volvemos a hacer notar que la medición de la captación de I-131 por la tiroides nos muestra solamente la avidez de la glándula por el yodo o sea una etapa en el metabolismo del yodo y que por consiguiente su valor aislado, no tiene valor diagnóstico patognomónico.

### Resumen

Se evaluaron 800 historias clínicas de pacientes del Hospital Universitario y del Municipal de Río Piedras y se analizaron 233 de éstos por tener cuadros clínicos bien definidos, encontrándose noventa y tres (93) eutiroideos que tuvieron una función tiroidea promedio de captación de yodo 131 a las 24 horas de 25.3% con desviación típica de 8.4 y rango y rango de 13.2 a 67.

Ochenta y cuatro (84) hipertiroideos presentaron un promedio de captación de yodo 131 de 69.1% a las 24 horas con desviación típica de 13.9% y rango de 31.6 a 97.

Sesenta y dos (62) pacientes con bocio no tóxico en los cuales el promedio de captación de I-131 a las 24 horas fué de 27.3% con desviación típica de 12.9 y rango de 7.7 a 81.9.

Veinticuatro (24) hipotiroides cuyo valor promedio de captación fue de 6.6% con desviación típica de 5.7% y rango de 1.1 a 20.7.

El 5% de los hipertiroides con valores bajos coincide con la zona de eutiroideos y el 5% de los eutiroideos con valores altos coincide con la zona de hipertiroides.

El 30% de los hipotiroides con valores altos coincide con la zona de pacientes eutiroideos y el 8% de eutiroideos con valores bajos coincide con la zona de pacientes hipotiroides.

Aceptando un promedio para los pacientes eutiroideos que van de 8 a 45% para la captación de I-131 a las 24 horas reclamamos una precisión diagnóstica de cerca de 95% para pacientes hipertiroides, 87% para eutiroideos y 70% para los pacientes hipotiroides.

### Summary

A total of 800 clinical histories of patients from the University and Río Piedras Municipal Hospitals were reviewed. Of these, 263 records contained adequate clinical data for clear cut clinical pictures of thyroid dysfunction. These group of 263 patients, yielded 93 euthyroid individuals with an average 24 hour I-131 uptake of  $25.3\% \pm 8.4$  (range 13.2 — 67); 84 hyperthyroid patients with average 24 hour I-131 uptake of  $69.1\% \pm 13.9$  (range 31.6 — 97); 62 subjects with nontoxic goiter with an average uptake of  $27.3\% \pm 12.9$  (range 7.7 — 81.9) and 24 hypothyroid patients with average uptake of  $6.6\% \pm 5.7$  (range 1.1. — 20.7).

Five percent (5%) of the hyperthyroid patients with low uptake values overlap with euthyroid values, while 5% of euthyroid patients with high uptake values overlap with the hyperthyroid range. In the other side of the scale, 30% of the hypothyroid patients with low uptake values overlap the hypothyroid range. If we accept the range 8 — 45% for euthyroid patients which includes 95% of all the euthyroid patients studied, then we may assume a diagnostic precision of approximately 95% for hyperthyroid patients, 87% for euthyroid function and 70% for hypothyroid function.

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## INFORME DEL PRESIDENTE DE LA AMPR

### Introducción:

Señor Presidente de la Cámara de Delegados, Compañeros:

Toca a su fin el año oficial 1963-64 de nuestra Asociación y con él mis obligaciones en la Presidencia. En este informe resumiré algunas de las gestiones más importantes que hemos llevado a cabo durante este año. Este ha sido un año extremadamente difícil, ya que no sólo tuvimos que enfrentarnos a los asuntos contenidos en las encomiendas y resoluciones de esta Honorable Cámara de Delegados, sino que también tuvimos que crear una organización administrativa enteramente nueva siete meses después de iniciar nuestra gestión presidencial. Aunque creemos que hemos llevado a cabo el programa de trabajo de nuestra Asociación, no por eso nos sentimos satisfechos con los logros obtenidos.

Nuestra encomienda llevaba como primer objetivo el implantar la reorganización administrativa según dispuesto por esta Honorable Cámara y poner en marcha el funcionamiento eficiente de los consejos y comités y el de renovar y ampliar los trabajos de las secciones de especialidad y las sociedades de distrito.

A raíz de renuncias inesperadas de todo el personal anterior, quedamos en una situación precaria. Gracias a la cooperación de los miembros de la Junta Directiva, de los consejos y de los comités, pudimos en corto plazo contratar el personal necesario para poner en marcha los asuntos de la Asociación una vez más. Es para mí motivo de gran satisfacción hacer constar que ya nuestra nueva organización está en plena marcha y trabajando incansablemente para poner al día todos nuestros asuntos.

Nos hemos dado cuenta también, en los últimos cuatro meses, que al aumentar su eficiencia nuestras oficinas han podido multiplicar el producto de sus trabajos. En un cálculo conservador, nuestras oficinas están atendiendo de ocho a diez veces más asuntos que en la época anterior. El producto de estas gestiones se nota en todas nuestras operaciones. Aquellas secciones de especialidad que han utilizado las nuevas facilidades disponibles han cobrado nueva vida, y muchas han iniciado planes de trabajo que necesariamente han de resultar en beneficio de todos nuestros miembros.

Para lograr este primer objetivo, hemos tenido siempre como meta el crear en nuestra Asociación una organización que de veras refleje la imagen del médico y que esté atenta y dispuesta a responder, no sólo a las necesidades de nuestros miembros, sino a todos aquellos problemas que afectan la salud de nuestro pueblo. Esto úl-

timo comprende el segundo de nuestros objetivos principales. Para llevarlo a cabo hemos representado la Asociación diligentemente ante las Comisiones de Salud y Beneficiencia de la Cámara de Representantes y Senado de Puerto Rico; ante la prensa, la radio y televisión para mantener informada la opinión pública; ante clubes cívicos: Rotarios, Leones, Exchange, etc.; y ante grupos de médicos y estudiantes de medicina. En esto hemos tratado de llevar la política y opinión sobre los distintos problemas establecida por esta Honorable Cámara.

Los informes que hemos hecho a la Cámara en sus reuniones ordinarias de abril y agosto de 1964 contienen una gran cantidad de información que documentan las motivaciones de las acciones tomadas durante el año. Al igual que entonces, incluimos en este informe el resumen de los asuntos más importantes para que, con vuestra consideración, se sugieran las acciones a tomar durante el nuevo año. Así éstos reflejarán el auténtico sentir de la clase médica, representada democráticamente por ustedes, miembros de la Cámara de Delegados.

### 1. Problema de la construcción de hospitales en P. R.

En el informe suplementario A aparecen las cartas dirigidas al Secretario de Salud, Dr. Guillermo Arbona, en las que puntualizamos nuestra posición de que la Junta Consultiva de Hospitales de Puerto Rico, que administra los programas federales para la construcción de hospitales, ha estado impropriamente constituida.

El doctor Arbona ha contestado todos nuestros argumentos diciendo que la ley pide que se dé una "consideración especial a hospitales que sirven una comunidad rural y de bajos ingresos." Usa esto como base para justificar el sistema de prioridades con que él asigna la distribución de camas de hospital en las distintas poblaciones de Puerto Rico. Hace algunos años el plan de hospitales para Puerto Rico decía que para nuestro propósito en Puerto Rico "no se designarían ninguna áreas rurales y que solamente se incluiría una región para toda la Isla". Esto fue así por "el tamaño pequeño de la Isla, por su sistema de carreteras, por la alta concentración de población y por la manera en que las viviendas están localizadas en su mayoría, cerca de vías de acceso". Sin embargo en años subsiguientes se sometieron planes estatales usando distintas áreas geográficas como "Regiones, Sub-Regiones y Areas". La manera en que él ha hecho caso omiso de las prioridades que él mismo ha designado es asombrosa. En lo úsltimos diez años la Sub-Región de Caguas ha tenido el por ciento menor de necesidades por camas de hospital satisfecha (15%), aunque se han construido allí 116 camas. En el mismo tiempo en la Sub-región de Fajardo, que ha teni-

do el % más alto de necesidades por camas de hospital satisfecha (84%), se han construído 95 camas adicionales. En el plan actual propuesto para el período desde 1965 a 1975, el doctor Arbona ha designado más áreas rurales; aunque, de hecho, todas las partes de nuestra Isla hoy día son menos "rurales" ahora que nunca.

Hemos exhortado al doctor Arbona a considerar los cambios definitivos que ha habido en la demanda por camas de hospital en Puerto Rico en los últimos diez años. Sus estadísticas le dicen que mientras el número total de ingresos a los hospitales de gobierno no ha disminuido, hay un aumento definitivo en el número total de admisiones a los hospitales de la comunidad. Esto se debe a varios factores:

1. El aumento en ingresos por familia y del ingreso por capital, de tal naturaleza que hoy día el 52% de nuestras familias pueden financiar los servicios médicos hospitalarios que necesitan. (El número de éstas aumentará sobre el 80% para el 1980.)
2. El aumento del número de personas acogidas a planes de seguro voluntario de salud prepagado.
3. El aumento en eficiencia en la utilización de camas de hospital de la comunidad y el aumento consecuente en la demanda en sus servicios.

El doctor Arbona sigue confuso en la política de continuar la construcción de pequeñas unidades de hospital de 8-10-20-30 camas en comunidades rurales según la ley que él cita. El debiera saber ya que las camas que existen en estos hospitales pequeños tienen una utilización de alrededor del 50%. Esto quiere decir que la mitad de ellas están vacías todo el año. El debiera saber que nadie puede operar un hospital pequeño eficientemente y que su construcción y operación sólo puede justificarse bajo circunstancias especiales en algunas regiones aisladas. Repetidas veces le hemos recordado que en vez de construir 6 hospitales pequeños en seis comunidades adyacentes, que se construya un hospital con alrededor de 150 camas que le pueda dar los servicios adecuados a esas comunidades.

Otro cambio significativo que se nota en el plan de hospitales es el que indica los cambios repentinos que se hacen en la clasificación de camas de hospital existentes de aceptables a no aceptables, dirigido a crear o eliminar las necesidades de un área en particular y cambiar las prioridades lo mismo en zonas rurales que urbanas.

El doctor Arbona es la única persona en Puerto Rico que asigna las prioridades para camas de hospital en cada región y el único que las cambia de año en año y el único que decide que todos los fondos federales disponibles de las leyes APW, Hill-Burton y Hill-Harris estarán disponibles para construir solamente hospitales de gobierno. Por eso él es el único que puede decirle que no a cualquier

grupo de la comunidad idóneo que está en la disposición de construir y operar un hospital de la comunidad sin fines de lucro y que no representaría gasto alguno para el gobierno del Estado Libre Asociado de Puerto Rico.

El es el único que puede decirle a ese grupo, cada vez mayor, de personas de ingresos moderados que no hay suficientes facilidades de hospital para atenderlos. De hecho, ya está preparándose legislación que le permitirá al gobierno cobrar por los servicios de hospital y médicos a personas pudientes y a los acogidos a seguros voluntarios. La mitad de esos hospitales (en centros de salud) están medio vacíos y no hay suficiente dinero para atender al pobre adecuadamente. Por eso se piensa que cobrándole al paciente en estos hospitales tendrían suficiente dinero para operarlos adecuadamente. El se olvida que la responsabilidad primaria del gobierno es la de cuidar debidamente al pobre. Esto no se puede hacer poniéndolo a competir con el rico por los servicios que necesitan en los hospitales de gobierno.

El paciente debe exhortarse a utilizar sus propios recursos. Como por naturaleza los servicios médicos hospitalarios son costosos, el gobierno debe ayudar a organizar grupos de la comunidad para fomentar la construcción de hospitales de la comunidad sin fines de lucro. De esta manera se pueden proveer los servicios de más alta calidad al costo mínimo. También debe el gobierno considerar que muchos de estos hospitales de la comunidad pueden hacerse cargo de atender las necesidades de los indigentes mediante programas en que el gobierno les ofrezca reembolsarles el costo auditado per diem. La filosofía de la utilidad del hospital de la comunidad sin fines de lucro, fue sabiamente prescrita en el espíritu y la letra de la ley federal y estatal que también le asigna la responsabilidad de mantener el delicado balance entre hospitales de gobierno y la comunidad a la agencia estatal que el doctor Arbona preside. El ha utilizado toda su autoridad para construir sólo hospitales de gobierno. Las excepciones que han permitido la construcción de un grupo pequeño relativamente de camas de hospital de la comunidad son pocas y escasamente representan el 11% de los fondos asignados a Puerto Rico. En el nuevo plan de hospitales discutidos recientemente en vista pública se dispone para la construcción de hospitales en los próximos diez años, la cantidad de \$210,000,000 y entre esto no se vislumbra la participación de hospitales de la comunidad.

Por estos motivos hemos hecho la reclamación a nombre de la comunidad al doctor Arbona diciéndole que al planificar para la monopolización de todos los fondos disponibles de programas federales para la construcción de hospitales de gobierno en efecto está llevando a cabo SOCIALIZACION SIN LEGISLACION.

Como la Junta Consultiva de Hospitales estaba impropiamente constituida, el doctor Arbona ante nuestro reclamo solicitó de nuestra Asociación se le sugiriese un candidato representativo nuestro como un grupo no gubernamental, nuestra Junta de Directores sometió el nombre de un servidor vuestro. Queda sin embargo, si se lleva a cabo este nombramiento por el señor Gobernador y la designación de tres otros representantes de "consumidores" que reemplacen aquellos miembros de la Junta que al presente representan agencias gubernamentales por ser altos oficiales de las mismas.

Aún constituida propiamente la Junta Consultiva de Hospitales de Puerto Rico queda por aclarar el problema fundamental de la política que gobierna la asignación de prioridades y que pueda permitir la consideración de la construcción de hospital sin fines de lucro por grupos de la comunidad.

La socialización de la medicina en Puerto Rico se decidirá en un futuro cercano en estos dos campos: 1ro. En el campo de los hospitales, sin legislación. 2do. En legislación dirigida para cobrar por servicios en hospitales gubernamentales a personas pudientes y con seguro.

## 2. Problema de Acreditación de Hospitales en P. R. y ECFMG.

Nos place informar que como resultado directo de las gestiones hechas por nuestra Asociación se pudo evitar la cancelación de los programas acreditados de internado en Puerto Rico, con excepción de los hospitales de distrito de Arecibo y Aguadilla. Se han reafirmado los acuerdos tomados por el Departamento de Salud en cuanto a mejorar los programas de internos y residentes en los hospitales acreditados. Se ha seguido una política clara en cuanto a mantener las normas de funcionamiento de hospital que permitan la acreditación de sus programas de enseñanza y que a la vez resultan en mejor calidad de atención a los enfermos. Nos place anunciar que se han dado pasos definitivos para mejorar las condiciones de los hospitales de distrito de Arecibo y Aguadilla y que por nuestro concurso la reinspección de estas instituciones por el Consejo de Educación Médica podrá llevarse a cabo en un futuro cercano con miras a restablecer la acreditación de sus programas de entrenamiento.

De acuerdo con nuestras sugerencias se han llevado a cabo dos cursos intensivos preparatorios para los médicos graduados en el extranjero que deseaban tomar el examen que ofrece el ECFMG y así acreditararse para poder hacer un internado reconocido. Todos los comentarios que han llegado hasta nosotros demuestran que es-

tos cursos han sido de un valor significativo y en muchas ocasiones, decisivo para aprobar el examen. Ya informamos cómo, para la convocatoria de abril tuvimos que hacer una visita a Chicago para lograr que admitieran a examen a unos 49 candidatos que habían sometido sus solicitudes tarde o incompletas. Gracias a la gentileza y comprensión del Dr. G. Halsey Hunt, Director Ejecutivo de ECFMG, y del Dr. W. Hubbard, Director Ejecutivo del National Board of Medical Examiners, logramos el favor especial para este grupo de candidatos. Recientemente para la convocatoria del mes de octubre intervinimos para que a unos 15 candidatos a los que les habían negado permiso para tomar el examen fuesen finalmente admitidos.

Dado el caso de que tantos compañeros médicos graduados del extranjero tienen dificultades al someter las credenciales para ser admitidos a este examen, sugiero que nuestra Asociación ofrezca a todos ellos un servicio de consulta y enlace con el ECFMG para tramitar todas las solicitudes y así evitar contratiempos de última hora. Hubo cinco candidatos que se presentaron a examen y no pudieron tomarlo por no tener la debida autorización. Esto representa una gran pérdida además de toda la angustia que ocasiona en la vida profesional de estos compañeros.

Estamos convencidos de la necesidad de continuar auspiciando estos cursos intensivos preparatorios para los compañeros graduados en el extranjero. Por lo tanto sugiero a esta Honorable Cámara reafirme su política a este respecto.

No empece todos nuestros esfuerzos de ayudar a estos compañeros graduados en el extranjero que están en Puerto Rico para tomar y aprobar el examen ECFMG, debemos considerar el problema ocasionado por este requisito de examen a los que aún están por graduarse con miras a estudiar a fondo este problema y presentarlo oficialmente ante las autoridades educativas de España. A tal efecto he nombrado un comité compuesto por el Dr. W. Benavent, Presidente de la Cámara de Delegados, el Dr. Lorenzo Galindo, el Dr. Juan Vilella, Presidente de la Asociación de Médicos Graduados de España, el Dr. Roberto Fumero, Presidente Electo de esta Sociedad, y los doctores Eduardo Medina, Luis Viñas Sorbá, Alfred Axtmayer, Carlos Guzmán Acosta y Adán Nigaglioni, miembros de esta Cámara de Delegados. Le sugiero a esta Honorable Cámara expresarse y respaldar esta acción. Este es un problema difícil que requerirá un cuidadoso estudio y acción prudente.

### 3. Comisión del Gobernador.

Los trabajos iniciados durante la presidencia del Dr. José S. Licha en julio de 1963, continuaron hasta marzo de 1964 y tras una ardua y difícil tarea se rindió un informe al señor Gobernador con

el concurso de todos los miembros participantes. La labor del doctor Licha durante su gestión presidencial fue muy destacada y sentó las bases para aclarar ante los miembros de la Comisión los difíciles problemas de salud en Puerto Rico. Luego que inicié mis trabajos en esta Comisión fui ayudado por el Dr. Egidio Colón Rivera.

Quizás entre los logros más destacados de esta Comisión fueron, el probar cómo, un grupo compuesto de altos oficiales del gobierno y de la comunidad pudieron laborar juntos para entender los problemas de salud de nuestro pueblo y unir sus ideas en un informe que contiene una serie de valiosas recomendaciones. Algunas de éstas se han puesto en práctica. La más importante hasta la fecha ha sido la de establecer incentivos adicionales al sueldo básico en un diferencial a determinarse a base de la dificultad de reclutamiento y retención para las áreas difíciles de servir y de ofrecer paga adicional por los trabajos hechos durante los turnos de guardia.

Una de las recomendaciones fundamentales de este informe es la que trata sobre la política pública referente a los servicios médico-hospitalarios y recomienda que ésta se haga clara y específica y que se cumpla estrictamente. Se indica que la responsabilidad pública primaria es al individuo de escasos recursos. Añade que el Gobierno no debe atender a ninguna persona con suficientes medios económicos para proveerse de servicios médicos privados, salvo en casos de emergencia. Se recomienda también, que a la mayor brevedad posible, se haga un estudio para determinar la capacidad económica de los pacientes que el Gobierno atiende y hasta qué punto el Gobierno está sirviendo adecuadamente a los que debe atender. La Comisión encontró una serie de deficiencias en la administración del programa de becas de estudiantes de medicina. Al igual que se encontraron ejemplos en el cual se habían otorgado becas hasta por 8 años, también encontró la necesidad de que el Departamento de Salud cumpla la responsabilidad de establecer un programa mediante el cual los becarios puedan cumplir los compromisos contraídos según requiere el contrato de becas.

La Comisión encontró que las condiciones en que se le pide trabajar al médico en muchas ocasiones son desfavorables. Se carece de facilidades adecuadas de vivienda y en muchos municipios no se conceden licencias por vacaciones. No existe un programa claro de trabajo ni de responsabilidades y deberes ni de turnos de horas en que el médico debe trabajar. Esto añadido al gran número de pacientes que acuden a los servicios municipales y a las escasas facilidades con que cuenta el médico para hacer su trabajo contribuyen a agravar la situación. No hay tampoco un programa defi-

nido que le permita al médico ampliar sus conocimientos y continuar su educación postgraduada para mantenerse al tanto de los adelantos de la medicina. Se encontró también que en muchas ocasiones se conseguían médicos que fueran a servir en estos pueblos, pero no se podían retener allí debido a las condiciones tan difíciles de trabajo. En un municipio en particular no se logra retener al médico aunque se le paga \$1,000 mensuales.

La Comisión se enteró de la labor de los médicos extranjeros acogidos a la ley 96 de 1963. A la vez que reconoce ésta la contribución de éstos, recomienda que es necesario que estos médicos comprobaron adecuadamente su capacidad profesional para garantizar una atención adecuada a los pacientes que atienden, y pide que estos médicos cumplan con los mismos requisitos que se les exige a los médicos puertorriqueños.

La Comisión hizo constar la necesidad de orientación adecuada a todos los sectores de la comunidad sobre los servicios médico-hospitalarios. Dió énfasis, a la necesidad de fomentar buenas relaciones de trabajo entre el alcalde y el médico para que pueda quedar definida claramente la función de ambos y así evitar la interferencia de lo administrativo en lo profesional.

Esta orientación general es necesaria también para exhortar al público en general la necesidad y las ventajas de voluntariamente proteger su salud con seguros médicos pre-pagados. Indica ésto, cómo una solución efectiva al problema de servicios médico-hospitalarios en Puerto Rico, ya que las proyecciones económicas en los próximos años hechas por la Junta de Planificación pondrán esta solución al alcance de un número cada vez mayor de personas. También recomienda la Comisión que el gobierno debe hacer estudios pertinentes para ofrecer, a los casos de beneficencia, servicios médico-hospitalarios por medio de seguros que ofrezcan libre selección de médico y hospital siendo la prima pagada por el Gobierno.

**La Comisión indica además, que es urgente que el Gobierno ayude a la realización de proyectos para el establecimiento de hospitales para la comunidad donde se requiera un mayor número de camas y le facilite el uso de los fondos provistos por la ley Hill-Burton o de cualquier otro fondo federal disponible.** Esta necesidad fundamental, como pueden ver ustedes, en esta recomendación fue comprendida claramente por todos los miembros de la Comisión.

Se recomendó finalmente, como el sentir unánime de los miembros de la Comisión, que existe la necesidad de crear una comisión al nivel estatal que sirva como cuerpo asesor al Gobernador y al Secretario de Salud. Aquí también se reconoce la contribución, que para mejorar los servicios médico-hospitalarios del pueblo y conse-

uir la participación de la comunidad en pleno, pueden hacer un grupo de ciudadanos interesados en estos problemas.

#### 4. Asociación Médica Americana.

Este año tocó a nuestra delegación emprender dos largos viajes a Portland, Oregón y a San Francisco, California para participar en los trabajos de la Cámara de Delegados de la AMA. La oportunidad de participar como una parte componente de esta Organización Nacional es una por la cual debemos estar profundamente agradecidos. En cada problema que se ha consultado hemos recibido siempre y en una forma gentil y considerada, ayuda y consejos efectivos. Nuestra labor en pro de solucionar los problemas anteriormente citados sobre la acreditación de nuestros hospitalares fue decidida favorablemente para nosotros gracias a la labor de nuestros delegados y de la disposición de la Junta de Directores de la AMA y los miembros de su Consejo de Educación Médica. Así mismo, conseguimos nosotros solucionar muchos de los problemas de nuestros compañeros con el ECFMG. La visita de los representantes de la División de Servicios en mayo pasado fue de un valor incalculable. Así también lo fue la reunión que celebrara el Consejo de Salud Ocupacional en enero pasado cuando se condujo un programa extenso dirigido a "Health and Safety for the Puerto Rican Workers" y que contó con la participación de representantes de la Asociación de Manufactureros, del Departamento de Salud y de las Uniones Obreras. Es triste pensar, sin embargo, que el número de nuestros miembros que pertenece a la AMA es tan pequeño. Estoy convencido de que esto se debe principalmente a la falta de organización que existía anteriormente. Recomiendo a esta honorable Cámara de Delegados que una vez más exhorté a todos nuestros miembros a pertenecer a la AMA y estoy seguro, que de así hacerse, con una campaña de reclutamiento hemos de obtener que un número crecido de nuestros compañeros se hagan miembros.

La muerte repentina del Dr. Norman Welch, Presidente de la AMA, hace dos meses representa una pérdida grande para la medicina libre en el mundo. Ha asumido la presidencia el Dr. Donovan F. Ward, quien nos visitará oficialmente el próximo martes. No empece los múltiples compromisos ocasionados por la muerte del doctor Welch, el doctor Ward accedió gustosamente a visitarnos y conocer sobre el terreno, más sobre los problemas de Puerto Rico. Así también se demuestra cómo la AMA cumple con sus compromisos con mucho más de lo que nosotros podemos ofrecer.

La AMA-Education and Research Foundation ha hecho posible contribuciones notables a la educación médica de Puerto Rico. Este

año entregamos un cheque a la Escuela de Medicina de Puerto Rico por valor de \$10,000. También hay un total de 164 estudiantes, internos y residentes, que han recibido préstamos por valor de \$222,000. Esta contribución efectiva incluye 85 préstamos a estudiantes de medicina de nuestra escuela por valor de \$115,000. Representa este programa un paso en firme hacia la solución del problema económico que tienen nuestros estudiantes, internos y residentes, y es prueba de lo que nosotros, los médicos, hacemos en pro de la educación de nuestros jóvenes. Le recomiendo a esta Honorable Cámara de Delegados que apruebe una solución exhortando a todos nuestros compañeros a participar en el programa de la AMA-ERF.

Ante la Cámara de Delegados de la AMA en su próxima reunión en Miami se ha de discutir extensamente el concepto de "Areawide Planning for Hospitals". Le recomiendo a esta Honorable Cámara de Delegados que prepare una resolución para ser sometida a la AMA en que basándose en nuestras experiencias sobre la planificación "compulsoria" de hospitales en Puerto Rico, reafirme su opinión clara y definitiva de manifestarse en contra y exhortar por la necesidad de que en la planificación de hospitales se utilice el concepto voluntario, que incluya la participación de representantes de la comunidad (incluyendo la Asociación Médica Estatal) además de incluir representantes de agencias de gobierno.

##### 5. Labor de las Secciones de Especialidad.

Hemos laborado intensamente porque todas las Secciones de Especialidad trabajen dentro del seno de nuestra Asociación, haciendo la labor científica y administrativa que les compete. Aunque en varios casos ellas están trabajando y llevando a cabo programas científicos de gran importancia para nuestra Asociación, hay algunas cuyas labores son muy limitadas y otras que no celebran reuniones de ninguna clase hace varios años. Durante este año se asignó una secretaría a cargo de los asuntos de la Secciones exclusivamente y aquellas Secciones que se han aprovechado de esta oportunidad están muy satisfechas porque han podido aumentar la cantidad de trabajo profesional que hacen. Algunas de las Secciones han estado trabajando sin reglamento y otras han modificado su reglamento sin haber sometido estos cambios para aprobación por esta Cámara de Delegados.

Hemos notado que algunas Secciones están afiliadas a "Sociedades" y todos los trabajos que desarrollan aparecen bajo los auspicios de las "Sociedades". Aunque no hay objeción principal para que los miembros de una Sección se constituyan a si mismos como

miembros de una Sociedad, es imprescindible que todas sus labores estén identificadas con la Sección.

En la reunión anterior recomendamos que se revisara el Reglamento disponiendo que todas las Secciones de Especialidad debieran tener su reunión anual administrativa para elección de funcionarios en o inmediatamente antes de la asamblea anual cosa de que la instalación de sus nuevas directivas coincidiera con la elección de los otros funcionarios de nuestra Asociación.

Recomendamos a esta Cámara de Delegados que suspenda temporeraente el endoso a las secciones que no hayan celebrado sus trabajos en los últimos años para considerar su creación de nuevo cuando un grupo de los especialistas correspondientes, se reúnan, preparen su reglamento y den evidencia de su interés de fundar la Sección dentro de las normas y procedimientos ya establecidos por esta Cámara.

#### 6. Sociedades de Distrito.

Hemos estado muy conscientes de la necesidad de atender los asuntos de nuestros miembros y de establecer vías de comunicación por las que podamos recibir de ellos la información pertinente y por la que podamos nosotros desde la Asociación central participarles de la manera como se están llevando a cabo los distintos programas y encomiendas de esta Cámara. Aunque, desde luego, es necesario que los miembros de la Junta Directiva y la Cámara de Delegados electos a nivel de distrito participen en todas las deliberaciones de la Junta Directiva Central y de la Cámara de Delegados y que al regresar a los distritos le comuniquen a sus miembros toda la información pertinente sobre los asuntos discutidos, la labor de la sociedad de distrito no empieza y termina asistiendo a reuniones. Para que las actividades de las sociedades de distrito sean de impacto en la opinión pública no sólo de los médicos sino del pueblo, se ha sugerido que deben llevar a cabo por lo menos ocho programas. 1) Un servicio de emergencia en que se dé a conocer al pueblo el sitio donde debe llamar para localizar un médico en caso de necesidad. 2) Un comité de enlace con el comité central de Mediación y Querellas. 3) Un programa continuo de relaciones con la prensa. 4) Un Foro de Oradores que sirva no sólo para participar en conferencias con grupos de la comunidad sino que organice una serie de cursillos dirigidos a nuestros miembros en que se traten todos los temas de ética, medicina socializada, servicios y ventajas que ofrece nuestra Asociación y que explique la política y posición de la AMPR en los problemas que afectan la salud de nuestro pueblo. 5) Un programa de orientación para nuevos miembros. 6) Un pro-

grama mediante el cual se garanticen cuidados médicos para aquellos que tienen limitaciones o no pueden pagarlos. 7) Un programa de servicios a la comunidad. 8) Un programa que demuestre nuestro interés en los asuntos cívicos.

Se ha traído ante la consideración de esta Cámara una enmienda al Reglamento en la cual se disponga que debe existir un minimum de miembros para que los médicos que residen en un grupo de pueblos puedan constituirse como sociedad de distrito. En la directiva según el reglamento indica, debe haber diez miembros que a su vez pertenezcan a esta Cámara. Si el número de médicos que componen un distrito es demasiado pequeño, la labor de la directiva solamente recae en unos pocos que tienen que servir año tras año y no les es posible a veces llevar a cabo todas las actividades necesarias. Los distritos más afectados por esta proposición de enmienda son los de Aguadilla (Noroeste), Mayagüez, (Oeste) y Arecibo (Norte). Ya los miembros de los distritos de Aguadilla y Mayagüez se han reunido y discutido extensamente este problema. Con la aprobación de los miembros y la directiva de estos dos distritos las organizaciones actuales de ambos se suspenderían y los miembros de este grupo de pueblos en conjunto han accedido a constituirse como un nuevo distrito y elegir una nueva directiva. Los 22 miembros del distrito de Aguadilla pasarían junto a los 81 miembros del distrito de Mayagüez a constituir un distrito de 103 miembros. Los 8 médicos que residen en Isabela y Quebradillas, que antes pertenecían al distrito de Aguadilla han expresado su deseo de formar parte del Distrito de Arecibo (Norte). (Véase informe del Secretario.)

El Distrito de Arecibo (Norte) solamente cuenta al presente con 64 miembros. Por eso será necesario que la enmienda propuesta al reglamento contenga una disposición la cual permita que los miembros del distrito de Arecibo aumenten el número total de sus miembros a 100, estipulando que deben hacer esto en un período de tres años.

Esta enmienda al Reglamento también permitiría que los médicos que residen en la parte Este de la isla desde Caguas a Fajardo a Yabucoa y San Lorenzo puedan solicitar a la Cámara, constituirse como distrito. Al separarse del distrito hoy denominado Este, se constituirían ellos como el distrito Este y el de San Juan como el Distrito Metropolitano, quedando esto a discreción de la Cámara de Delegados.

Vislumbramos para el futuro cercano que la adecuada organización y trabajos de las sociedades de distrito compuestas con suficientes miembros, permita la participación de un mayor número de compañeros para llevar a cabo nuestras actividades y así se hará

sentir mejor el deseo y se cumplirán las necesidades de nuestros miembros en todos los pueblos de la isla.

**7. Entrevista con el Dr. Harold M. Granning "Assistant Surgeon General, Chief Division of Hospitals, Medical Facilities, USPHS.**

Doctor Granning met with us last Friday afternoon October 30, after visiting all week long 19 hospitals and related facilities throughout Puerto Rico which had been built with federal funds. He told us that he had selected 14 of them before coming and the rest were selected by doctor Guillermo Arbona's office. He explained to us that his inspection visit was to determine whether these hospitals were being maintained properly and were being utilized adequately thus serving the function intended in their planning. Although he was to report his findings to doctor Arbona later, we believe that he confirmed our findings that the majority of hospitals in health centers and other government institutions are not maintained or utilized properly.

Doctor Granning commented at length on the authority, duties and composition of the Hospital Advisory Council (HAC) to the State Agency. He indicated that although the Council in Puerto Rico has been "legal", it must be changed completely if it is to meet the requirements of the new Hill-Harris ammendments. Thus no government official and no one connected directly with a hospital its board of trustees, health insurance plan executives or physicians could qualify under the heading of members representing "consumers". For each one of its members named by the governor representing a governamental agency or a nongovernamental organization there must be one representing the "consumers" (by public representatives such as ministers, bank executives, industrialists, etc., without any ties to government or health organizations).

Before any State Plan can be approved, doctor Granning's office will require a statement over the governor's signature indicating that new Commonwealth legislation will be presented next January that will comply with these new federal regulations.

More revealing, however, were his comments on the Puerto Rico State Plan for 1965. You may recall it was discussed at Public Hearings in August 21 and that it contains 10 year projections for the construction of \$210,000.00 worth of hospital and medical facilities, all in government institutions. This plan is now obsolete as it was done through Hill Burton Advisory Council which expired on June 30, 1964. (I never quite understood why doctor Arbona

held public hearings on the basis of a law that had expired. He could not have followed the new Hill-Harris Ammendments because President Johnson did not sign the appropriations bill until September and doctor Arbona had not fulfilled the requirements to set up the new Hospital Advisory Council.) It is then up to a new properly constituted Council to study the needs for hospitals here. Now doctor Arbona must recommend to the Governor, candidates to properly constitute the Hospital Advisory Council and stop padding it with government officials (including his wife's brother in law). Also, the entire policy governing priorities must be revised. Hospital bed utilization together with demonstrated need and ability to operate and maintain facilities adequately will replace the arbitrary designation of beds per 1000 population. This fits in with everything that the Puerto Rico Medical Association has been saying all along.

Doctor Granning expressed his opinion that he is convinced that there must be consideration given to the construction of non-profit community hospitals in Puerto Rico as the best solution to the needs for hospitals care to middle income groups. There are great hopes that with a new Hospital Advisory Council, properly constituted with lay representation, a careful revision can be made of existing policy. His office cannot force the Council to decide that all funds be used for government institutions or all for nonprofit ones. This is a decision for the Council but doctor Granning can and has advised that there should be proper balance between both considering true needs impartially. He also said that although doctor Arbona as head of the State Agency could submit a plan not approved by the Councils, his office would not approve it. There would be no need for an Advisory Council as set up in the law if the State Agency would not pay attention to it and it would be foolish for a Secretary of Health not to follow the Council's advise. Remember that with the old Hospital Advisory Council, all the plans and decisions made by doctor Arbona were rubber stamped by his padded council.

We are grateful for doctor Granning's initiative in coming to Puerto Rico and find out for himself so that he can shed new light on the problem. We are also hopeful that a change for the better is in the offing. Doctor Arbona has recently asked us to submit a slate of candidates to the new Hospital Advisory Council for consideration for appointment by our governor.

#### 8. Plataforma de Salud.

Este año fue necesario que nuestra Asociación participara en el desenvolvimiento político de nuestro pueblo ofreciéndole a los par-

tidos políticos nuestras ideas sobre la programática que debe contener una plataforma de salud desde el punto de vista imparcial y no partidista, ya que es política fundamental de esta Asociación el pensar que la solución de los problemas de salud del pueblo no conoce límites de partido ni puede estar sometida a peticiones partidistas. La salud es parte esencial del derecho humano si se ha de reconocer la dignidad del hombre en una verdadera gran civilización. En el último informe a esta Cámara le incluimos el texto de nuestra declaración sobre Salud.

Nuestra actividad en el campo político no termina en el año electoral sino que tiene que continuarse constantemente para así mantener informada no solamente la opinión pública sino a todos aquellos que tienen la responsabilidad de legislar o administrar los programas de salud. Esta participación política de parte del médico puede ser efectuada individualmente en el partido de su elección. También es necesario que el médico individualmente participe en la vida política y cívica de nuestro pueblo.

#### 9. Relaciones Públicas.

El Programa de Relaciones Públicas en nuestra Asociación es uno de los más importantes y durante este año no sólo hemos tratado de estar atentos a establecer buenas relaciones con los miembros de las Cámaras Legislativas, los miembros de otras asociaciones profesionales, la Escuela de Medicina y sus estudiantes, el Departamento de Salud y sus dependencias, los clubes cívicos del país, la prensa, radio y televisión sino que hemos desarrollado un programa intensivo para mejorar nuestras relaciones con los médicos que componen nuestra Asociación. Para esto hemos contado en parte con la colaboración del Dr. Luis F. Sala y su Consejo de Relaciones Públicas. También nos han ayudado en una forma notable nuestros asesores en Relaciones Públicas de la firma Publicidad Badillo, los Sres. Samuel Badillo, Gustavo Agrait y Julio Rivera. La contribución de estos últimos en reuniones semanales y a veces con más frecuencia ha sido definitivamente un factor decisivo para llevar a feliz término nuestra representación ante el público. Aunque queda todavía mucho por hacer, compartimos con estos compañeros la gran satisfacción de ver cómo han mejorado nuestras relaciones públicas y como así se ha adelantado para proyectar la imagen del médico y de nuestra Asociación. Quedan todavía algunas personas que guardan algunos prejuicios. La presentación clara y desinteresada de la política establecida por esta Cámara de Delegados ha sido posible gracias al concurso de nuestros asesores. Hemos aprendido que no empece lo mucho que tenemos que decir de nuestros asuntos hay que saber cómo decirlos y cuándo decirlos. Exhorto a

esta Cámara de Delegados a extender nuestras felicitaciones por la labor prestada a nuestros asesores de Relaciones Públicas.

#### 10. Tribunal Examinador de Médicos de Puerto Rico.

La labor del Tribunal en este último año ha sido extremadamente difícil. En la convocatoria de marzo examinó a 161 candidatos y en la de septiembre a 183. Esto significa que prácticamente se ha duplicado el número de médicos que comparece a examen. Por este motivo también ya no se pueden utilizar las facilidades de nuestra Asociación para conducir el examen y se utiliza en vez el local del Colegio de Ingenieros que aunque más amplio no es adecuado. El premio que otorga nuestra Asociación al candidato que obtenga el promedio más alto en los exámenes de reválida le toca este año a dos compañeras que empataron. Son ellas las doctoras Engracia Truyol y Carmen Feliciano.

Tanto para la convocatoria de marzo como para la de septiembre solicitó un grupo de médicos acogidos a la ley 96 de 1963 que se les permitiera tomar la primera parte del examen de reválida. Por nuestra parte notamos con gran placer que un grupo significativo de ellos haya expresado su deseo de completar el examen regular de reválida. Es nuestro sentir sin embargo al igual que el de innumerables compañeros que se han dirigido a nosotros, que tenemos duda sobre si el Tribunal tiene autoridad para permitirle a estos médicos extranjeros tomar esa primera parte del examen cuando a la vez que no lo autoriza la Ley 96 tampoco lo autoriza la ley regular número 22 por requerir esta última la ciudadanía antes del examen. En el informe suplementario B aparecen las cartas dirigidas a nuestros asesores legales y su contestación sobre este asunto. Fue al conseguir esta opinión legal que el Tribunal acordó dejar sobre la mesa la consideración de los resultados de los exámenes que en esta última convocatoria de septiembre habían tomado un grupo de médicos extranjeros hasta tanto se hiciese la consulta correspondiente al Secretario de Justicia. No podemos predecir en el momento qué condiciones jurídicas, si alguna, se produciría cuando estos médicos tomen y aprueben la primera parte del examen de reválida. Es claro, sin embargo que entre ellos haya un grupo que desea comprobar su capacitación completamente y al igual que todos nosotros lo hemos hecho bajo la ley regular. Es claro también que lo correcto sería que estos compañeros médicos extranjeros presentaran su problema ante la Asociación Médica de Puerto Rico, el Tribunal Examinador y el Departamento de Salud para que se hiciera un análisis objetivo y cuidadoso de todo este asunto. Una de las conclusiones posibles a considerarse sería la de ir juntos ante las Cámaras Legislativas y solicitar una enmienda a la Ley 96 para

que esta exija como requisito todos los exámenes comprendidos en la reválida bajo la ley regular y así dejar probada su competencia al igual que nosotros. A considerarse también sería una enmienda a la ley la cual les permita a aquellos que en el futuro fueran naturalizados ciudadanos, llenar todos los requisitos para ejercer la medicina libremente en Puerto Rico. Me permito sugerir a esta Honorable Cámara que designe una comisión para que de inmediato estudie esta situación y que recabe la participación del grupo de médicos extranjeros acogidos a la Ley 96 que estén interesados, el Tribunal Examinador de Médicos, y el Departamento de Salud.

La posición de la Asociación Médica de Puerto Rico debe afirmar los principios básicos contenidos en la ley 22 que regula la práctica de la medicina en Puerto Rico requiriendo además de una adecuada preparación universitaria y profesional, la ciudadanía, cualidades morales y de buena conducta; la comprobación de su competencia profesional mediante exámenes de reválida completos. No debe esta Asociación en ningún momento aceptar una disminución de esos criterios si ha de velar por la buena práctica de la medicina y por la protección de la salud del pueblo.

Queda aún pendiente la selección por el Sr. Gobernador del candidato que sustituya al Dr. A. S. Casanova Díaz de la terna que le fuese enviada y mientras tanto continúa en funciones este último. Vuestra Junta de Directores tomó nota de que el nombramiento del doctor Casanova había terminado en septiembre del año pasado. Se envió una terna compuesta por el Dr. Enrique Vicéns, Dr. Luis F. Sala y el Dr. Alfred Axtmayer.

Deseo recordar a todos los compañeros Delegados que es también obligación nuestra mantenernos al tanto de todas las decisiones del Tribunal e informados de sus problemas.

## 11. Quackery

Nos queda todavía mucho por hacer en cuanto a librarnos al pueblo de las graves consecuencias que resultan de las prácticas de los curanderos, santiaguadores, espiriteros, quiroprácticos y otros charlatanes que se aprovechan de personas ingenuas para con toda manera de engaños y promesas falsas engañarlos. A principio de año comparecimos ante la Comisión de Salud y Beneficencia de la Cámara de Representantes cuando se nos solicitaron comentarios al P. de la C. 911 que enmendaba el artículo 1 de la ley 78 que regula la práctica de la técnica radiológica. Favorecimos entonces, esta enmienda que específicamente excluye a los quiroprácticos de tener licencia como técnicos radiológicos y de tener en sus oficinas como empleados dichos técnicos ya que no se les reconoce su

capacidad para manejar el equipo de Rayos X ni su capacidad para interpretar los estudios radiológicos. Esta enmienda fue aprobada. Además solicitamos que se enmendase la ley 493 de 1952 que regula el ejercicio de la quiropráctica en Puerto Rico para eliminar de ella todas las cláusulas absurdas que contiene y ponerle fin a las prácticas indeseables de esta seudociencia. El detalle de este informe está incluido en el folleto de la Cámara del pasado abril.

El tercer principio de ética de nuestra Asociación dice que el médico debe practicar aquel método de curación que está fundamentado en una base científica; y que no debe voluntariamente asociarse profesionalmente con ninguna persona que viola este principio. Entendemos que es prácticamente imposible para el médico que observa nuestros cánones de ética como las guías de su conducta que se asocie o fraternice con estos curanderos o quiopráticos. Es inconcebible que pueda separarse ante la opinión pública la asociación personal o fraternal del médico de la profesional, cuando éste alterna con esos curanderos y se pone en lugares en que pueda aparecer citado o retratado en la prensa. Es con mucho pesar que hemos notado que algunos compañeros han sido víctimas de esa situación y le hemos referido a nuestro Comité de Etica el análisis cuidadoso y objetivo de estos casos. Nosotros estamos en la obligación de tener mucho cuidado cuando participamos en actividades de sociedades benéficas relacionadas con la salud de que en ningún momento se pierda de vista el principio de ética envuelto y quedemos atrapados en situaciones comprometedoras cuando estos curanderos o quiopráticos logran por osadía y afrenta ser incluidos en las directivas de estas asociaciones.

Es necesario dar énfasis a la importancia de mantener la dignidad de la medicina y de sostener la pureza y las enseñanzas científicas como opuestas a las falacias de estos cultistas y charlatanes. O las teorías y prácticas de la medicina científica son las correctas y la de los cultistas las incorrectas; o la de los cultistas son correctas y las de la medicina científica son las incorrectas. El médico que mantiene relaciones con cultistas practicantes aparecería como exhibiendo una falta de fe y convicción en la veracidad y eficacia de la medicina científica y como admitiendo que hay mérito en los métodos de los cultistas.

Es necesario que en el futuro, nuestra Asociación preste una mayor atención a las prácticas de estos charlatanes en defensa de la salud del pueblo. El problema es difícil ya que estos cultistas poseen una sagacidad y habilidad para convencer con sus mentiras y engaños a muchos incautos y toda acción de nuestra Asociación debe estar fundamentada en la verdad y en la razón, utilizando prudentemente todos sus recursos para educar al pueblo y orientarlos para que sepa protegerse mejor.

## 12. Fundación Médica de Puerto Rico

Ya empieza a rendir frutos la labor de la Fundación Médica. Se ha preparado un folleto que expone los motivos de su existencia para enterarlos a todos sobre la Fundación. Les exhorto a que contribuya cada uno de acuerdo con su capacidad para que el crecimiento de la Fundación cuente primero con la contribución de la clase médica. El doctor Licha ya ha preparado otro folleto informativo para los estudiantes de medicina que estudian en universidades extranjeras en el que se explica cuáles son los requisitos que ellos deben cumplir para practicar la medicina en Puerto Rico y aclara muchas preguntas y dudas que han causado contratiempos. Estamos seguros que este folleto será muy útil y orientará debidamente ya que cuenta en su preparación con el endoso del Departamento de Salud, el Tribunal Examinador de Médicos de Puerto Rico y nuestra Asociación. La Asociación de Esposas de Médicos nos ha dado un donativo de \$1,500 destinado al programa de becas de nuestra Asociación. Durante la Sesión Inaugural el próximo martes haremos entrega de estos fondos a la Fundación Médica quien llevará a cabo nuestro programa de becas para estudiantes de medicina, junto con una contribución de nuestra Asociación.

## 13. Aborto Criminal

Como resultado de la lucha que ha librado nuestra Asociación en los últimos años para combatir la práctica del aborto criminal en Puerto Rico, conseguimos que se enmendase la ley para que se requiera a todo médico y hospital hacer un informe oficial al Departamento de Salud cuando atienda cualquier caso de aborto. También se eliminó el requisito en la ley que exigía la presentación de prueba de que la mujer estaba embarazada y se hizo igualmente culpable a cualquier otra persona que ayude al aborcionista.

Estamos convencidos de que la mayoría de las mujeres que acuden al aborcionista criminal no se dan cuenta de la gravedad del mal que hacen. Cuando un ladrón roba, y destruye el producto robado para que no se conozca su falta no está de hecho, cometiendo un grave mal adicional. Pero cuando la mujer trata de eliminar la criatura que lleva en el vientre para esconder su culpa de relaciones ilícitas o de temores fundados en ansiedades materialistas no se da cuenta de que lo que está haciendo es un crimen más grave que la falta que cometió inicialmente. El aborto criminal es un crimen tan horroroso porque escoge la víctima más indefensa y destroza y mutila despiadadamente la criatura para robarle el derecho de nacer.

Es con gran pesar que hemos notado como últimamente va en aumento notable el número de veces que se nos informa por nues-

otros compañeros que alguna mujer continental les ha solicitado le practique un aborto criminal. Es de conocimiento de todos nosotros que cualquiera de estas personas que vienen del continente pueden obtener los nombres y direcciones de los sitios donde se llevan a cabo estas prácticas criminales. Cualquiera desde el aeropuerto puede conseguir la información necesaria y conducirse hasta las dos o tres personas que están siempre dispuestas por dinero a complacerlas. También la información se consigue en los taxis, en los hoteles, en algunas farmacias y desgraciadamente también algunos médicos aunque no practican el aborto están por un precio dispuestos a referirle el caso al aborcionista.

En repetidas ocasiones nos hemos reunido con el Secretario de Salud y el Secretario de Justicia para exhortarlos a conseguir una solución a este problema. La ayuda que hemos recibido de estas agencias no ha sido efectiva. En este año los casos llevados a corte en que médicos eran acusados de practicar abortos salieron absueltos. El único que puede resolver este problema en Puerto Rico es el Secretario de Justicia utilizando todos los recursos de su departamento para hacer una investigación exhaustiva cosa que no le será muy difícil. Para esto estoy seguro que podrá contar con la ayuda de la Asociación Médica de Puerto Rico. Mientras el Departamento de Justicia no se disponga a hacerle frente a las tres personas que sabe todo el mundo se dedican al aborto criminal, estos seguirán aumentando diariamente su macabra clientela. No debe ser muy difícil tampoco para el Departamento de Justicia y para el Departamento de Hacienda hacer una investigación sobre los ingresos de estas personas. Una de ellas se estima gana más de un millón de dólares anuales.

#### 14. Sears Foundation

Por invitación, el Presidente de nuestra Asociación, forma parte del "Medical Advisory Board" de la Sears Foundation y como tal ha participado desde hace 2 años en sus reuniones. El programa principal que se ha desarrollado es el que ayuda a ciertas comunidades a establecer facilidades adecuadas para atrer uno o varios médicos a estos sitios donde se hace difícil reclutar y retenerlos. Esto se hace de una manera que genera todos los recursos de la Comunidad para resolver sus problemas de salud y ha tenido un éxito notable. Recordamos este programa a nuestros compañeros ya que si alguno en Puerto Rico está interesado le podemos ayudar en este propósito.

La Sears Foundation también contribuyó enormemente con su entusiasmo, asesoramiento y sus contribuciones económicas a la creación de nuestra Fundación Médica. Le recomiendo a esta Honorable Cámara le extienda a la Sears Foundation un voto de agras-

decimiento por su contribución al desarrollo de planes en favor de la salud de nuestro pueblo.

### 15. Auxilio Médico Mutuo

La Junta del AMM ha estudiado intensamente el programa de beneficios a nuestros miembros. Después de haber sometido nuestro plan a revisión por los actuarios consultores (Candelas y Queipo) ha aconsejado que se enmiende el Reglamento para reducir los beneficios a un nivel actuarialmente factible. La Junta también ha considerado varias proposiciones de compañías de seguros pero recomienda que lo indicado al presente es continuar nuestro plan con beneficios reducidos.

La Junta del AMM se ha convencido que nuestro plan equivale a un seguro de vida **permanente**. Por esa razón la Asociación debe separar una parte de la cuota que actuarialmente acumule valores equivalentes a los beneficios a pagarse. Los miembros que han participado del plan desde su comienzo en 1942 han contribuido en estos 22 años el total de \$437.50. Nuestros actuarios sostienen la opinión que \$27.00 por miembro al año no es suficiente para ofrecer beneficios de \$3,000.00 cada uno e indican que sólo puede pagarse \$2,000.00 a los que han pertenecido a nuestra Asociación por más de 8 años y \$1,000.00 a los que lo han sido por menos.

En este manual se les acompaña una copia del informe de nuestros actuarios. También explican que esta cantidad de beneficios es posible solamente si se cobran las cuotas a tiempo y se ponen a producir intereses. Les exhorto a estudiar cuidadosamente el informe de los actuarios y asistir a la Asamblea Extraordinaria el próximo sábado.

### 16. Boletín

Nuestra Junta Editora ha hecho una labor magnífica durante este año y recomienda que se aprueben las nuevas partidas para gastos del Boletín durante el próximo año ya que se ha de duplicar su tamaño y su circulación. También están desarrollando planes para mejorar la calidad de impresión y hacer un nuevo formato.

### COMISION DE COSTOS Y DISTRIBUCION DE SERVICIOS MEDICOS

El informe del Comité que nombrase esta Cámara de Delegados el pasado agosto para estudiar este problema ha revelado una serie de datos de suma importancia. Es sumamente revelador que

el Indice de Precios al Consumidor de Servicios Médicos en Puerto Rico haya aumentado un 40% en comparación con el costo de vida general, que aumentó 125%. Se demuestra cómo de hecho ha bajado el porciento del salario gastado por servicios médicos. También es muy revelador que casi el 50% de los gastos en servicios médicos no gubernamentales fueron para compra de medicinas, lo que indica una frecuente automedicación.

Toda acción gubernamental sobre problemas de salud estará decidida a base de los factores de costo y distribución de servicios. Por eso es tan necesario que nuestra Asociación utilice todos sus recursos para estudiar estas fases del problema y esté debidamente preparada para la presentación de su plan de servicios después de someterlo al más cuidadoso y minucioso estudio. Recomiendo que esta Cámara ordene la creación de una Comisión de Estudio de Costo y Distribución de Servicios Médicos que actualice los estudios del Informe Turssel de 1959 y utilice como guía los hechos recientemente por la A.M.A. Sólo con la información correcta y al día podemos basar nuestras acciones futuras.

#### **Beneficios a Miembros:**

Es un placer anunciarles que la S.S.S. ha formalizado un plan grupal de hospitalización para nuestros miembros. De esta manera tendremos una protección adecuada a un bajo costo para casos de necesidad entre nuestros compañeros.

También en adición a este plan, nuestra Junta de Directores aprobó un plan grupal de "Major Hospital Expense Insurance" con la I.N.A. (Insurance by North America) que complementa con protección adicional hasta \$10,000 con un deducible de \$500, también a un precio módico. Este plan incluye hasta \$1,500 maximum por el tratamiento de enfermedades mentales.

Exhortamos a todos los compañeros Delegados a comprar esta protección tan necesaria hoy día y aconsejar a nuestros compañeros a así hacerlo también. La S.S.S. tiene un sitio entre las exhibiciones técnicas para hacer todos los contratos.

#### **Consulta al Secretario de Hacienda:**

En el informe suplementario transcribimos la copia de la Consulta que hicieron al Honorable Jorge Font Saldaña, Secretario de Hacienda, sobre los requisitos que debe llevar una constitución de hospital para merecer exención contributiva. Les llamó la atención en particular al inciso f, donde indica que no se puede restringir el uso de sus facilidades a un grupo particular de médicos.

## 17. Estado actual de nuestra Asociación y proyecciones al futuro

Nos damos cuenta clara al estudiar los informes de nuestro Secretario, Tesorero y otros que la labor realizada por nuestra Asociación es posible, gracias a la participación y sacrificio de un gran número de compañeros. Ellos toman una parte activa al conducir nuestros trabajos. Aunque nuestra labor fue detenida por motivos ya conocidos durante los primeros 7 meses de este año, y por 2 meses más por contratar y entrenar nuevo personal hemos sentido una honda satisfacción al ser testigos del ver despertar un entusiasmo genuino por muchas de nuestras Secciones de Especialidad, Consejos, Comités y Sociedades de Distrito. Este entusiasmo se ha traducido también a muchos miembros que encuentran en nuestra reorganización nueva vida y calor. Algunos de los que se habían dado de baja han solicitado reingreso al ver nuestro progreso. Nuestro continuo progreso y futuro está en vuestras manos. Está de nuestra parte contribuir con una participación activa y palpitante o escoger quedarnos sólo como observadores de los acontecimientos del futuro. Está en nuestras manos y corazones la participación en la solución de los problemas de la salud del pueblo.

Ha sido necesario tomar decisiones que cambiaban costumbres anteriores, especialmente aquellas que fueron necesarias para obedecer nuestra Constitución y Reglamento. Se han establecido prácticas administrativas claras y eficientes en los asuntos económicos. Se han tratado de cobrar las cuotas adeudadas y se han reclasificado correctamente muchos de nuestros miembros afiliados a activos y viceversa. Hemos cambiado la forma de presentación del presupuesto. Aquí se incluye un presupuesto para noviembre y diciembre de 1964 para que la nueva Junta Directiva pueda llevar a cabo sus asuntos sin preocupaciones. El nuevo presupuesto del 1965 incluye operaciones para los 12 meses naturales que coinciden con el año de cuota y de ingresos. Todo queda basado en el año natural con excepción del examen de operaciones por nuestros auditores externos, "Haskins & Sells", que se prepara a septiembre 30 e informar a la Cámara.

La nueva agrupación de las Sociedades de Distrito, de aprobarse, indudablemente mejorará sus trabajos y el producto de sus esfuerzos será mayor. Al igual, si se aprueban las enmiendas para que coincida la elección de funcionarios a ellas y a las secciones de especialidad, se podrán coordinar los trabajos eficientemente.

Si en algo han mejorado nuestras oficinas centrales, es importante que éstas continúen ampliando sus operaciones para que

respondan adecuadamente a nuestras necesidades. Tiene que continuarse una supervisión continua.

Hoy día tenemos poco más de 1400 miembros. Han ingresado 147 médicos este año y quedaron 27 solicitudes en trámites. Nuestra matrícula comprende el 60% del total de médicos en Puerto Rico (2,300). Estimamos que de los 900 médicos no socios, unos 300 internos y residentes o en espera de aprobar su reválida y unos 400 otros trabajan a tarea completa en el gobierno. El Tribunal Examinador expide un promedio de 160 licencias al año. De seguir este ritmo, habrá en Puerto Rico para el año 1974 unos 4000 médicos.

Debemos prepararnos para conducir una campaña vigorosa para atraer la mayoría de los que hoy no son miembros y de los que han de venir en el futuro para en 10 años sobrepasar el 75% de socios y tener sobre 3000 miembros en nuestra Asociación. (Recordemos que en el 1954, contábamos con 660 miembros de los 1289 médicos en Puerto Rico, operábamos con un presupuesto de \$32,670.00 y teníamos 7 empleados).

¿Cuánto ha de significar para nuestra Asociación poder participar en este precimiento? ¿Cómo podemos prepararnos para absorber una matrícula dos veces mayor que la presente? ¿Cómo podremos nosotros atender las necesidades de nuestros médicos y responder al reclamo de la comunidad en los problemas de Salud? ¿Qué ha de significar para nosotros el cambio continuo necesario para este progreso? ¿Cómo podemos adaptarnos a estos nuevos problemas? Estas, y muchas otras interrogantes podemos entretener en nuestras mentes. Estoy seguro, sin embargo, que comparten conmigo todos ustedes, el deseo de formar parte de ese futuro, que ya sea reservado para nosotros la culminación de nuestras esperanzas o la desilusión, nunca tendremos el ánimo corto y frustrado y conservaremos la alteza de espíritu, la confianza en la razón y la verdad y el respeto por la dignidad del hombre libre.

Deseo expresar mi profundo agradecimiento a todos los compañeros que de una forma u otra hicieron posible lo que se ha hecho este año. Tengo la obligación de significar la ayuda de mi predecesor y consejero, Dr. José S. Licha, Presidente Saliente y maestro de presidentes. También debo singularizar mi agradecimiento a todos mis compañeros en la Junta Directiva, y en particular al Dr. Enrique Vicéns por su incansable e inagotable fuente de estímulo y esperanzas. Al Dr. Héctor Bladuell le expreso también mi agradecimiento porque fue un fiel y leal compañero, constantemente a mi lado a través de los momentos más difíciles con su comprensión profunda y su consejo acertado y a tiempo y por sus preguntas claves. Deseo hacer constar además, mi gratitud personal al Dr. Egidio S. Colón Rivera, nuestro Presidente Electo,

quien cooperó grandemente al éxito de mi gestión presidencial. Desde ahora le ofrezco reciprocar en lo que pueda por todas sus atenciones. Finalmente a todos ustedes que por ventura o desventura me concedieron la oportunidad de servirles con lo mejor de mi ser.

Cordialmente,

**Carlos E. Bertrán, M.D.**  
Presidente

## DISCURSO DEL PRESIDENTE DE LA AMA

### WE MUST SERVE - TOGETHER

DONOVAN F. WARD, M.D.

President, American Medical Association

It is "con mucho gusto" that I appear before you tonight, to bring you the greetings of 200,000 of your colleagues in medicine, the members of the American Medical Association. Even after a few short hours on your beautiful island, your kind hospitality has made a deep impression on Mrs. Ward and me. We hope to see much and meet many of you before we leave.

As we were flying in, looking down on Puerto Rico sparkling in the blue waters, the pilot announced that your mean temperature here is 76 degrees. Let me assure you, ladies and gentlemen, that if you have ever spent a winter in the midwestern United States, there is certainly nothing "mean" about a temperature of 76 degrees! Our January mornings often find the thermometer at minus 20, and that, amigos, is a "mean" temperature!

As a visitor it would be presumptuous of me to pretend to bring you anything more than the greetings I have presented . . . that plus a desire to learn as much as possible about the excellence which signifies Puerto Rican medicine.

But I can tell you that the AMA sincerely wishes to be of service to you whenever and wherever possible. To that end, at this moment there is a group of three very capable representatives of the AMA here in Puerto Rico. They have come to meet with you and to study the problems you report concerning Hill-Burton and Kerr-Mills programs on the island. They are here because you have asked the AMA House of Delegates to consider resolutions concerning these problems. When they return with their findings we can act knowledgeably and hope to cooperate intelligently. We can take another step in the unity that is so vital to medicine if it is to fulfill its trust to humanity.

Unity in medicine. This was the singular goal of my dear friend, Dr. Norman A. Welch who assumed the Presidency of the AMA last June and who died just ten weeks later.

In his inaugural address in San Francisco, Dr. Welch asked for a professional unity which would transcend all barriers — barriers of geography, of personal interests; barriers between town and gown and particularly the barriers with which the specialist too often cuts himself off from the rest of organized medicine.

It was not a self-centered unity that Dr. Welch sought, nor was it to be based purely on defense of our views. Rather, it springs

from the fact that each of us must be responsible for the science, the art, and the socio-economic aspects of medicine.

Each of these three areas directly affects the patient and thus it **must** concern you and me, the physician. If I care for his physical needs without concern for socio-economic problems which influence his mind and body, then I am naive in pretending I am giving him full care.

Or, if I permit those who pander to his vote or his buying power to dictate the care I will provide him, then I am equally remiss in my sworn obligation to care for the whole man.

If, as a faculty member, I believe that pure medicine exists only within the groves of Academe then I am unrealistic. Or if, as a practicing physician, I see the medical school and the research institution merely as steps in my past, with no practical value to the "real world" of medicine, then I have failed to realize how deeply interdependant are town and gown. Without the teaching institution there could be no one to practice medicine. Without the physician in full-time practice, there would be no need for the teaching institution.

And if I, as a specialist, devote my full attentions to my field to the exclusion of my district or commonwealth medical societies, then I cut deeply into the unity of medicine as a whole. This is demonstrated by the specialist when he is asked to take part in medical society activities unrelated to his specialty. It is then that some excuse themselves from these responsibilities by contending that medical organizations should confine their interest and activities to the science of medicine.

Wherever medicine has fallen under the yoke of government dictation, it has come about because it lacked the unity it should have. It lacked a spokesman and it lacked the shared interest of its members. The theory of divide-and-conquer is effective again and again, and it has proven to be effective against our own profession. History is the best teacher.

These are important reasons for increased unity among all who practice medicine. Yet there is an even **more** substantial reason. That is that only through mutual cooperation do you and I continue to grow in stature and ability as physicians. This is an amazing day in which we live. In the Americas, we have learned more medicine and techniques in the past quarter-century than man has learned in the previous two thousand years! Who among us finds that each day gives us enough time to absorb what is being offered us? Who knows all that he believes he should? Who has time to read all that is germane to his field to improve his technics to add to his armamentarium?

New knowledge is being spread farther and faster all over

the globe... by individual physicians, medical missionaries, medical associations and journals, technical assistance programs, and international health organizations.

Generally speaking, the people of the world today are living longer, suffering less from infectious diseases and malnutrition, and enjoying better health. Although a tremendous amount of work remains to be done, scientific cooperation has brought heartening progress in applying the tools of public health, medical care disease prevention, nutrition and related fields.

All over the world, the dramatic scientific developments in medicine have stimulated mounting public interest in health and medical care. This interest, more and more, extends not only to scientific advances but also to the various socio-economic aspects of medicine about which we spoke. People everywhere want the best possible answers to the questions of how to organize, provide and finance modern medical services so that they are more readily available to millions.

Because of these facts, the everyday demands on you and me as physicians are much different than they were ten years ago, just as they have increased upon everyone involved in the advance of medical science . . . educators, researchers and organizations.

At the very time that medical science is becoming more complex, more difficult to keep abreast of, we are being called upon to expand our vision, both as physicians and as citizens. No longer is ours an ivory-tower profession, well-insulated from world affairs. It has truly become one of the great functions of modern civilization. Our responsibility now is to see that it fulfills that function to the maximum degree, for the benefit not only of the health of our people and of the world but also for peace, as well.

Through unity and cooperation, our medical societies and our colleagues offer to us learning which no one of us could assimilate in a lifetime of private labor. From laboratories, medical centers, classrooms, surgeries and private offices throughout most of the world, these bright chains of knowledge come down through our societies, our medical journals, our colleagues, to benefit us and our patients. What a tragedy, when there is so much to know and so little time that some would weaken or break those chains through indifference.

Indifference and withdrawal from the medical community are the principal causes of the break in its unity. But conversely, and happily, an increase in activity on the part of any one of us, adds a strength which cannot be measured, for that strength goes out in waves throughout our entire profession.

Those waves must continue to emanate, throughout our profession and throughout the world. Ours is the one field dedicated

solely to the preservation of life! What a wonderful responsibility that is, but how terrible the consequences if we neglect it.

There are many who say that communism will win the world through default unless free peoples move more rapidly unless we more thoroughly demonstrate and share the benefits of freedom. We in medicine must take our part in this sharing.

We must share our knowledge and our resources because they are good —good for the individual, his nation and the world. With the help of good government, he in turn will work to solve his socio-economic problems through education, health, a desire for achievement and the opportunity to compete in a free society. But he cannot gain these ends without one basic quality —his health. And he will not enjoy that health to its fullest unless each of us works together in humility and full cooperation.

May I suggest one form of that cooperation, and, to me, a very important form? May I suggest membership in the American Medical Association. Only 11% of your members hold membership in the AMA. How happy we would be and how much we would all benefit if we could bring to our rolls that remaining 89%. The AMA is the largest medical society in the world. Bigness is not necessarily effectiveness, of course, but I think it is safe to say that ours is also one of the most effective in the world. Through our Journal, through the more than 1,000 scientific meetings which we sponsor or co-sponsor annually, and through 164 committees on scientific and socio-economic matters, the AMA brings to medicine the newest and best work of the finest minds in medicine.

All of medicine would be fortunate if we could add to that chain of knowledge the contributions of Puerto Rico's physicians. We warmly invite you to join us, to take part in our operation, to attend our meetings —the next of which is our Clinical Convention in Miami, from November 29 through December 2. Come with us, work with us, and share with us the unity which we **must** have if medicine is to continue to grow in service to mankind.

**BOLETIN**  
DE LA  
**ASOCIACION MEDICA**  
DE  
**PUERTO RICO**

*Organo Oficial de la Asociación Médica de Puerto Rico*

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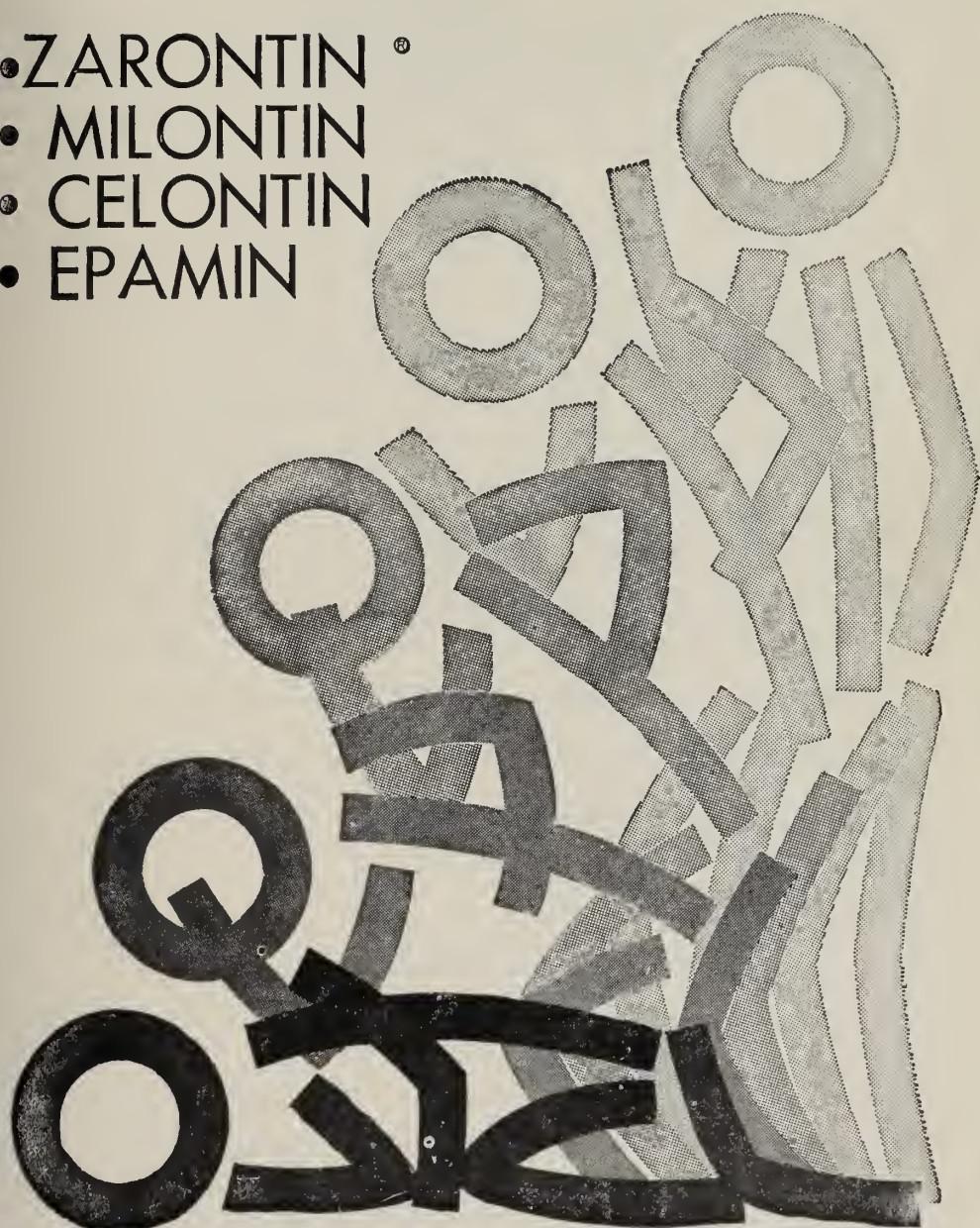
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# TERAPEUTICA ANTIEPILEPTICA COMPLETA

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## THE PROPERTIES OF OLIVE OIL

by Dr. F. María Segovia de Arana

"Thus, olive oil is unique among vegetable oils by reason of its organoleptic characteristics. Its natural aroma and taste are regarded pleasant by the consuming public in all countries. It need not be refined: it is the only oil that can be consumed in the West in its natural state. This is most important, because in the course of refinement, oils are to some extent transformed and lose some of their nutritive properties."

### COMPOSITION AND CHEMICAL PROPERTIES OF OLIVE OIL

"In the chart below, taken from Hilditch (The chemical constitution of natural fats) the composition in saturated fatty acids (miristic, palmitic and stearic and non saturated (oleic and linoleic) of olive oil in various countries is shown.

#### OILS.

	Miristic	Palmitic	Stearic	Oleic	Linoleic
Italy (Tuscany)	1,1	9,7	1,0	79,8	7,5
Córcica	1,1	9,4	2,0	84,5	4,0
California	1,1	7,0	2,3	85,8	4,7
Spain	0,2	9,7	1,4	81,6	7,0
Tunis	1,1	14,7	2,4	70,3	12,2
Palestine	0,5	10,0	3,3	77,5	8,9
Greece (Rhodes)	0,4	19,7	0,3	69,6	10,4

As can be seen, olive oil, apart from containing a large proportion of a non saturated fatty acid, of twofold linkage, namely oleic acid, also contains lesser quantities of others that have more than a twofold linkage."

## PHITOSTERINES

"Olive oil contain "phitosterine", which, as its name indicates consists of vegetable sterines similar to the colesterine of animal fats, but with the interesting biological characteristic that they are not absorbed by the wall of the stomach and what is even more important, that they prevent, to a greater or lesser extent, the intestinal absorption of the colesterine contained in food, as has been recently demonstrated by the experiments carried out by the Chaikoff School in the United States."

## ARTERIOSCLEROSIS AND OLIVE OIL

"The experiments carried out by Dr. Bronte Stewart in South Africa, demonstrated that colessterol in the blood increased when the subjects consumed animal fats, but this did not occur with vegetable fats, such as sun-flower oil, olive oil, etc.

The same type of result was achieved by a group of investigators (among others, Dr. P. D. White, President Eisenhower's personal physician, and Dr. Keys) in a test carried out in Calabria and Crete on subjects whose ages varied between 45 and 65 years and the fatty part of whose food consisted almost entirely of oil. Only two out of the 657 persons examined were seen to have had heart attacks. When this group was compared with a similar one, as regards age, in the United States, whose diet largely included large quantities of animal fats, sixty cases of heart attacks were discovered.

("Time" magazine, 30 December 1957)."

## CONCLUSIONS OF THE WORK OF DR. SEGOVIA DE ARANA

"We must be careful and only recommend such things as can reasonably be expected to do more good than harm. In our opinion, the following measures are reasonable and well founded:

- 1) Reduce the total consumption of calories and in particular those derived from fats, to the amounts consumed, (and which quantities should be maintained) when the body weight is normal between twenty one and twenty five years of age. It is advisable to use non saturated vegetable oils in lieu of animal fats.
- 2) Take active daily physical exercise.
- 3) Avoid all excess (tobacco, alcohol, emotional tension) but such habits need not be cut down drastically.
- 4) Treat arterial hypertension if it appears."

"Through the courtesy of Torres & Riballes, S. A., Seville, Spain, proprietors of the famous Spanish Olive Oil brand **BETIS**"



**Butazolidin**® brand of phenylbutazone  
Tablets of 100 mg.

**Butazolidin®  
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Each capsule contains:  
phenylbutazone, 100 mg.  
dried aluminum  
hydroxide gel, 100 mg.  
magnesium  
trisilicate, 150 mg.  
homatropine  
methylbromide, 1.25 mg.

**It works!**

Proved by over a decade  
of clinical experience.

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Ardsley, New York



not all but *Most*  
bacterial respiratory  
tract infections  
yield to ➤

therapeutically  
the *Most* active  
erythromycin



In the patient, Illosone *eradicates*, rather than merely inhibits, streptococci and pneumococci. This increased action is due to the fact that more erythromycin reaches the infection site because Illosone (1) is acid stable in the stomach, even in the presence of food, and (2) is better absorbed from the intestine.

Illosone produces peak levels of antibacterial activity *two to four times* those of other erythromycin preparations. Furthermore, these peak levels are attained earlier with Illosone and are maintained much longer.

**Side-Effects:** Even though Illosone is the most active oral form of erythromycin, the incidence of side-effects is very low. Infrequent cases of drug idiosyncrasy, manifested by a form of reversible hepatic dysfunction, with or without clinical jaundice, have been reported. There have been no fatal or definite residual effects. Gastro-intestinal disturbances are observed in a small proportion of individuals as a result of a local stimulating action of the medication on the alimentary tract. Cutaneous manifestations

of hypersensitivity may be observed occasionally. In extremely rare instances, anaphylaxis has occurred following the use of erythromycin.

**Usual Adult Dosage:** 250 mg. every six hours.

**ILOSONE®**  
(erythromycin estolate, Lilly)

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## WHY DOES ONE ANTIBIOTIC GIVE UP TO 2 EXTRA DAYS' ACTIVITY?

Because it is more resistant to disintegration, has a lower renal clearance rate than earlier tetracyclines...a favorable depot effect resulting from protein binding and greater mg. potency...all giving higher, sustained *in vivo* activity which continues long after the last dose.

# DECLOMYCIN<sup>®</sup>

## DEMETHYLCHLORTETRACYCLINE HCl

**Effective** in a wide range of everyday infections—respiratory, urinary tract and others—in the young and aged—the acutely or chronically ill—when the offending organisms are tetracycline-sensitive.

**Side Effects** typical of tetracyclines which may occur: glossitis, stomatitis, proctitis, nausea, diarrhea, vaginitis, dermatitis, overgrowth of nonsusceptible organisms. Also: photodynamic reaction (making avoidance of direct sunlight advisable) and, very rarely, anaphylactoid reaction. Reduce dosage in impaired renal function. The possibility of tooth discoloration during development should be considered in administering any tetracycline in the last trimester of pregnancy, in the neonatal period, and in early childhood. Capsules, 150 mg. and 75 mg. of demethylchlortetracycline HCl. Average Adult Daily Dosage: 150 mg. q.i.d. or 300 mg. b.i.d. 1. Kunin, C. M.; Dornbusch, A. C., and Finland, M.: Distribution and Excretion of Four Tetracycline Analogues in Normal Young Men. *J. Clin. Invest.* 38:1950 (Nov.) 1959.

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